American Journal of Obstetrics and Gynecology

VOL. 40 SEPTEMBER, 1940 No. 3

Announcement

The October issue of the JOURNAL will commemorate the twentieth anniversary of its establishment as an organ of publication in the domain of American obstetrics and gynecology. This special issue will present a series of brief, critical articles by a selected group of contributors, based on the developments during these past two decades in the fields to which the JOURNAL has been devoted.

We bespeak the attention of our readers to this anniversary number.

Original Communications

RETRODISPLACEMENT OF THE UTERUS IN RELATION TO PREGNANCY*

WITH SPECIAL REFERENCE TO THE TECHNIQUE AND END RESULTS OF THE BISSELL OPERATION

ALBERT H. ALDRIDGE, B.S., M.D., F.A.C.S., NEW YORK, N. Y.
(From the Clinic of the Woman's Hospital)

IN VIEW of all that has been written regarding the management of retrodisplacement of the uterus, one feels rather compelled to justify an effort to arouse the interest of gynecologists to reconsider the success and logic of accepted methods of treatment. If there is any justification for further discussion of this subject it is because:

1. Retroversion of the uterus will probably always be one of the more common gynecologic conditions requiring treatment and surgical intervention for the cure of symptoms in some cases.
2. Differences of opinion still exist as to indications for treatment of retroversion by both palliative and surgical means.
3. Follow-up records show that every retroversion operation in use at present, carries with it a definite although perhaps small percentage of surgical failures.

*Read at a meeting of the Chicago Gynecological Society, April 19, 1940.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

In the past twenty-five years, certain clinical observations have influenced the attitude of obstetricians and gynecologists as to the importance of retrodisplacement of the uterus as a clinical entity. Within this time we have acquired more exact knowledge of the relationship of retroversion to sterility. Obstetricians have become less concerned regarding the progress of pregnancy in a retroverted uterus and have found that under such circumstances the use of the pessary is rarely indicated. Realization of the fact that a high incidence of congenital backward displacements of the uterus occurs in all classes of women, has influenced many gynecologists and obstetricians, perhaps unwisely, to disregard symptomless postabortal and post-partum retroversion. Sampson's classic studies on endometriosis have aroused the interest of gynecologists in the possibility that retroversion, especially when associated with stenosis of the cervical canal, may favor the development of this serious condition. Follow-up studies have compelled gynecologists to be more careful in their selection of patients for whom relief of symptoms by surgical means seems indicated. To avoid the embarrassment of failing to cure preoperative symptoms and especially backache, more patients are being subjected to routine orthopedic examinations and therapeutic tests with retroversion pessaries to be sure that the backache and other symptoms of which they complain are really gynecologic in origin.

Finally, after extensive clinical experience, some gynecologists are doubtful as to whether retrodisplacement of the uterus, of itself, is ever responsible for physical symptoms. They are convinced that symptoms usually attributed to retroversion are almost invariably due to commonly associated functional and pathologic conditions of the cervix and uterine adnexa.

In relation to pregnancy, retrodisplacement of the uterus and the conditions associated with it present a threefold problem, because together they constitute an important etiologic factor in the causation of sterility, a common cause of abortion and conditions frequently responsible for unpleasant postabortal and post-partum symptoms. From a study of the relationship of retroversion and its associated conditions to pregnancy, it seems certain that the same underlying disturbances of function may be responsible for either sterility or early abortion.

Authorities are agreed that in the examination of women who seek advice on account of sterility, approximately 10 per cent will be found to have backward displacements of the uterus.

In the past it was believed that some women who had uncomplicated retroversion, were sterile because the cervix was turned forward out of the pool of semen and that for this reason proper insemination failed to occur. It is still considered that fertilization is more likely to occur if the development and position of the cervix are such that ejaculation of semen is directed into the external os of the cervical canal.

Comparatively recent observations, especially those in the field of endocrinology, have served to focus our attention on other important causes of sterility and early abortion. As a result of these observations,

the disturbances in function of the pelvic organs which may be associated with retroversion are better understood.

Retrodisplacement of the uterus is invariably accompanied by prolapse of the uterine adnexa, retardation of circulation in the blood vessels of the broad ligaments and some degree of chronic passive congestion of the uterus, tubes, and ovaries. Lacking proper nutrition, ovarian function is impaired. Normal maturation and rupture of some of the Graafian follicles may fail to occur; the ovaries may become cystic and the endometrium is frequently found to be hyperplastic. The common occurrence of menstrual disorders in the presence of chronic retroversion can be readily explained by interference with the process of oogenesis and the inevitable disturbances in ovarian hormone production.

Under such circumstances, it is believed that factors which contribute to the causation of sterility and early abortion are:

1. A reduction in the total number of normal ova produced.

2. Production of imperfect ova which either cannot be fertilized or, if fertilized, are cast off early in pregnancy because they lack qualities necessary for mature development.

3. An abnormal endometrium which predisposes to abortion because proper nidation of the fertilized ovum fails to take place.

In the presence of uncomplicated chronic retroversion, the lumina of the Fallopian tubes are often occluded or obstructed. This may be due to various causes, such as, angulation, thickening of the mucous membrane lining of the tubes as a result of congestion and hyperplasia, adhesions from healed endosalpingitis and plugs of mucus within the lumina.

Furthermore it is believed that the conditions associated with retroversion reduce local resistance of the abdominal pelvic organs to infection. Peritoneal adhesions and tissue damage resulting from healed inflammations add to the incidence of tubal occlusion and obstruction found in the examination of these cases.

In a small series of sterility patients operated upon for uncomplicated retroversion at the Woman's Hospital, 42.8 per cent showed tubal occlusion or obstruction when examined before operation, although the tubes appeared to be normal at time of operation. Rubin[1] reports that "tubal obstructions were met with in 66 per cent of backward displacements" of the uterus.

From all that is known regarding the relationship between uncomplicated retroversion and sterility, it is obvious that the most important objective physical finding is the frequent occurrence of interference with tubal patency. Certainly no sterile woman who has a retroversion can be considered to have been properly examined to determine the cause without having had a test for tubal patency.

It is an accepted fact that many women conceive readily in spite of backward displacements of the uterus. Undoubtedly in these women ovarian function has not been seriously disturbed and the patency of the Fallopian tubes has not been affected by the existing misplacements. When, notwithstanding the retroversion, menstrual periods are normal

and the tubes are found to be normally patent, it is quite probable that a thorough investigation will reveal other causes for a sterile marriage.

For sterile women with retroversion who have definite disturbances of the menstrual cycle and evidence of tubal occlusion or obstruction, active treatment is indicated. Menstrual symptoms may be relieved; tubal patency may be restored and conception may be allowed to occur if the uterus can be held in normal position by a well-fitted retroversion pessary. If the uterus cannot be replaced or if treatment with a pessary fails to give the desired result after a reasonable period of time and the husband has been found to be fertile, treatment of the retroversion by surgical means is usually indicated. At operation peritoneal adhesions or other pelvic pathology, which could not be made out by bimanual examination, may be found.

In discussing the conditions responsible for sterility, in relationship to uterine retroversion, attention has been called to certain factors which, under the same circumstances, are believed to predispose to early abortion. There is another small group of cases in which pregnancy in a retroverted uterus may be disturbed by the fact that the uterus fails to spontaneously assume a forward position as pregnancy advances. This is because it is either adherent to the peritoneum of the pelvis or because it becomes incarcerated in the hollow of the sacrum. Under such circumstances, the uterus can usually be dislodged with gentle bimanual manipulation. Occasionally this can best be done with the patient well relaxed under surgical anesthesia. Peritoneal adhesions will usually soften and give way as the uterus enlarges. Rarely is operation necessary to release such adhesions.

In recent years there has been an increasing tendency for many obstetricians to disregard asymptomatic post-partum retroversion. There are probably two important reasons for this change of attitude, namely,

1. Experience has shown that a considerable percentage of such retrodisplacements are either congenital in origin or the result of conditions which have caused chronic retroversion before the onset of pregnancy. It is an accepted fact that under such circumstances, a cure of uterine backward misplacements cannot be effected by palliative means.

2. With the adoption of delivery by prophylactic forceps after perineal incision as an almost routine procedure by many obstetricians, the great majority of women are left with perineal bodies and vaginas which closely approximate the nulliparous state.

Even though an episiotomy wound has healed normally, sufficient distention of the vaginal introitus to allow manual replacement of a retroverted uterus and insertion of one of the retroversion pessaries of the Smith or Hodge type, is usually accompanied by considerable discomfort for at least two to three months after delivery. For this reason obstetricians are reluctant to subject their patients to the discomfort of such treatments unless there are symptoms which cannot otherwise be relieved. They prefer to omit treatment with pessaries in the hope that when involution is complete, nature will have corrected those misplacements which have resulted from conditions associated with the pregnancies recently terminated by various methods of delivery.

It is probably fair to state that the only circumstances in which retroversion pessaries are useful in preventing chronic retroversion are after abortion and in the post-partum period. By relieving tension on the relaxed musculofascial supports of the uterus, normal involution is allowed to occur and physiologic function of the supporting structures of the uterus is thereby restored. Under all other circumstances, a retroversion pessary acts simply as a splint to hold the uterus in anterior position with the hope that symptoms caused by the condition will be relieved.

If obstetricians fail to take advantage of the most favorable opportunities to treat retroversion, namely, after abortion and in the post-partum period, it is possible that some women may be subjected to the necessity for subsequent gynecologic treatments or operations which might have been avoided.

It seems entirely justifiable to disregard an asymptomatic postabortal or post-partum retroversion if it is known that the uterus was retrodisplaced before the onset of pregnancy. However, many women never submit to pelvic examination until they are six to eight weeks pregnant. It is known that a backward displacement of the uterus, if discovered then, may be due to conditions associated with early pregnancy.

It is an admitted fact that many uteri found misplaced following abortion or delivery will be spontaneously restored to normal position when involution is completed. However, if there is no proof that retroversion preceded pregnancy, it seems wise to institute treatments, such as suitable exercises, vaginal douches and artificial means to support the uterus while involution is in progress. There is evidence to prove that such measures tend to promote proper involution of the pelvic organs and to reduce the incidence of permanent backward displacements.

It may be worth while to call attention to an ingenious pessary devised by Findley.[2] This pessary is a modification of the Smith type, in which a section of flexible rubber has been vulcanized into both its anterior and posterior margins. By this change in construction, it is possible to fold the pessary so that it may be inserted with no more distention of the vagina than is required for examination with one finger. From experience in the use of this pessary it seems certain that it supports the uterus as well as the one originally devised by Smith.

The most frequent indications for surgical treatment of retroversion will occur in women who have associated functional and pathologic conditions of the pelvic organs causing a variety of symptoms, such as pelvic pain, menstrual disorders, and backache. These symptoms may be caused by chronic passive congestion of the pelvic organs, cystic ovaries, healed inflammatory disease, or neoplasms involving the uterus, tubes, and ovaries.

A great majority of the women requiring such operations are within the childbearing period. Operative procedures to cure the conditions should be selected because they are conservative and because they are the ones best suited to withstand the test of future pregnancies.

It is probably fair to state that general surgeons and most gynecologists regard the surgical treatment of retroversion to be simple, reasonably successful and perhaps settled.

The result of any gynecologic operation to be regarded as entirely satisfactory should mean that preoperative symptoms have been relieved, that normal anatomic relationships have been restored and that normal function of the organs or parts involved is to be expected. On this basis it is obvious that surgeons lack confidence in the success of operations being done for retroversion probably because they not infrequently fail to withstand the most important test of function, namely, pregnancy. Otherwise, how can we explain the fact that so many patients that come for the relief of retroversion symptoms have been advised, even by gynecologists, to postpone treatment by surgical means until they no longer anticipate subsequent pregnancies? If a woman accepts this advice it may mean that she must either undergo a prolonged course of gynecologic treatments or endure her symptoms and some degree of physical disability for a number of months or years.

Therefore it would appear that there is still need for an operative technique which will re-establish physiologic function of the structures which support the uterus in a normal anterior position and in a way that is morely likely to withstand the conditions associated with pregnancy.

In the annals of gynecologic history, the year 1940 might very well be regarded as the one hundredth anniversary of the development of the first surgical technique for the cure of retroversion. Records show that it was in 1840, exactly 100 years ago, that Alquié[3] suggested the first definite plan whereby this condition might be treated by surgical means. Since that time, well over 100 retroversion operations have been devised. The treatment of retroversion is no exception to the rule that, when many techniques are advised for the surgical cure of any condition, none is likely to be uniformly successful as to results.

In recent years, significant changes have occurred in our approach to many gynecologic problems. Routine follow-up studies have demonstrated the necessity for modifications of many accepted gynecologic operative procedures in order to reduce the incidence of unsatisfactory end results. This is particularly true as regards operations for the repair of vaginal birth injuries and those for the cure of uterine prolapse.

If we study the improvements in technique that have been devised, we can hardly fail to realize that they have been made possible through a more exact knowledge of the anatomy and physiology of the pelvic organs and a better understanding of the musculofascial structures which are necessary to support these organs in normal position. For instance it has been found that uniformly satisfactory end results in the cure of vaginal birth injuries cannot be had by working with superficial denudations of vaginal mucous membrane in geometric patterns. No longer is it necessary to interpose the body of the uterus between the bladder and anterior vaginal wall to cure a large cystocele. For the surgical treatment of a prolapsed uterus we no longer depend upon a technique which fixes the fundus to the anterior abdominal wall. Provided there is no justifiable reason for removing such a uterus, the modern acceptable technique to cure the condition is one which aims to

re-establish its normal supports by repairing the damaged or overstretched so-called cardinal or Mackenrodt's ligaments.

In other words it is obvious that progressive improvement in the results of our gynecologic operative procedures has been accomplished by adopting modifications in technique and new methods which are based upon sound anatomic and physiologic principles.

From a study of the operative techniques which have been recommended for the cure of retrodisplacements of the uterus, by the abdominal route, we can hardly fail to be impressed with the ingenuity of some surgeons who have developed such procedures. In modern times, surgeons attempt to select the technique best suited to the conditions present at time of operation. They almost invariably employ one of five methods which are well known by the names of the surgeons who devised the procedures, namely, Gilliam, Montgomery-Simpson, Webster-Baldy, Coffey and Olshausen. The fundamental principle underlying all of these procedures is some scheme for shortening the relaxed round ligaments. In some instances, these operations are combined with surgical techniques for shortening the uterosacral ligaments and procedures to give additional support to the prolapsed uterine adnexa. In a small percentage of cases, retrodisplacements of the uterus are treated by techniques which permanently fix the fundus to the anterior abdominal wall.

The advantages and disadvantages of all these methods are too familiar to members of this society to require any comment.

From our knowledge of pelvic anatomy, it is known that all the pelvic organs are surrounded and supported by a thin layer of fascia, known as the endopelvic fascia. At the level of the internal os of the cervix, the uterosacral, cardinal, and pubocervical ligaments form a continuous plane of tissue which serves to support the nonpregnant uterus in a normal, more or less constant position as regards its level in the pelvis and the relationship of the cervix to the pubis, sacrum, and lateral walls of the true pelvis. This layer of tissue, often referred to as the upper pelvic floor, is a part of the endopelvic system of fascia.

Backward displacements of the uterus and prolapse of the uterine adnexa are prevented by normal function of the round and broad ligaments. The round ligaments are composed essentially of smooth muscle and the broad ligaments contain two layers of fascia derived from the endopelvic fascial system.

The frequent occurrence of congenital retroversion is often attributed to the fact that, through the processes of evolution, women have acquired an upright posture which has entirely changed the mechanical principles involved in the function of the musculofascial structures which support the uterus and the uterine adnexa.

From the location and anatomic construction of the broad ligaments it seems reasonable to assume that nature has intended that they have an important function in maintaining the normal anterior position of the uterus. It is interesting to note that with none of the more popular operations for the cure of retroversion is reconstruction of the relaxed

broad ligaments considered an important feature of the technique. In the Coffey operation, the proximal ends of the broad ligaments are incidentally folded over and sutured to the anterior surface of the uterus. With other operations such as Montgomery-Simpson and Webster-Baldy, puckering of some of the tissues of the broad ligaments necessarily occurs as the round ligaments are shortened. This may result in slight increased tension of the broad ligaments when healing is complete.

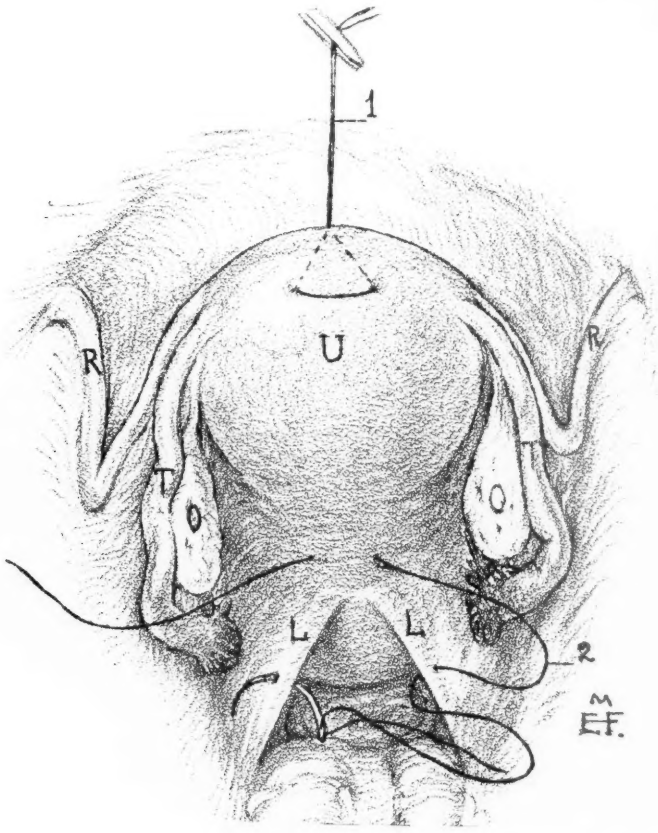


Fig. 1.—Shows the uterus, *U*; tubes, *T*; ovaries, *O*; round ligaments, *R*; and uterosacral ligaments, *L*. The uterus is being pulled forward by a chromic catgut No. 1 suture (*1*), which is used for traction during the operation and finally as a means of temporarily suspending the uterus to the anterior abdominal wall. Also shows a linen suture (*2*), which has been passed through the posterior surface of the uterus (*U*), and the uterosacral ligaments (*L*) in accordance with the technique recommended by Noble for shortening these ligaments.

In 1901, the late Dr. Dougall Bissell, attending surgeon at the Woman's Hospital, who was always deeply interested in the character and function of the structures which support the uterus, devised a surgical technique for the cure of retroversion by which both the broad and round ligaments could be shortened. In an article published in 1916,[4] he described the technique that had been developed and reported his results in 185 patients who had been operated upon. Having followed many of the patients for long periods of time and some through subse-

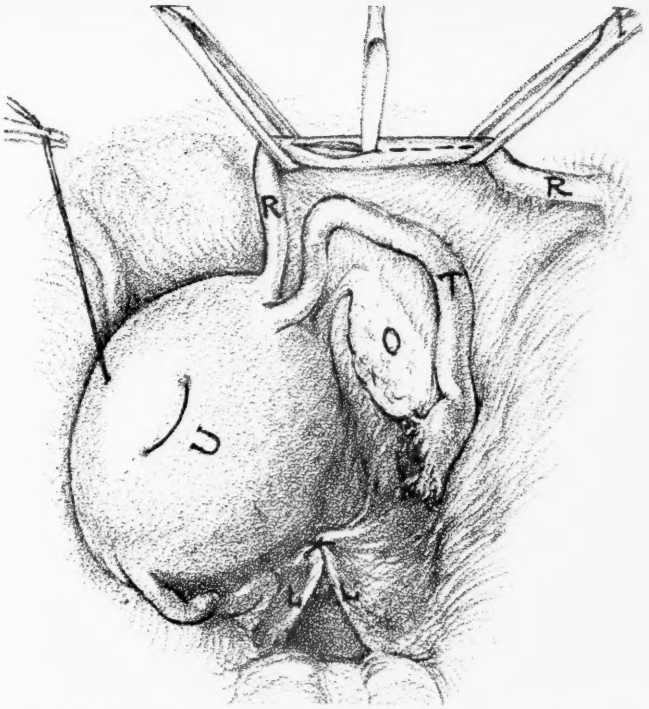


Fig. 2.—Shows the linen suture in the uterosacral ligaments (*L*), tied and the ligaments shortened. The uterus (*U*) is being drawn to the left side. The middle third of the round ligament (*R*) is being held under tension with two Allis clamps (*I*) so that it can be split longitudinally exactly in the midline throughout its entire thickness. This procedure is used as a means of approach to the avascular space between the two layers of endopelvic fascia contained within the structure of the ligament.

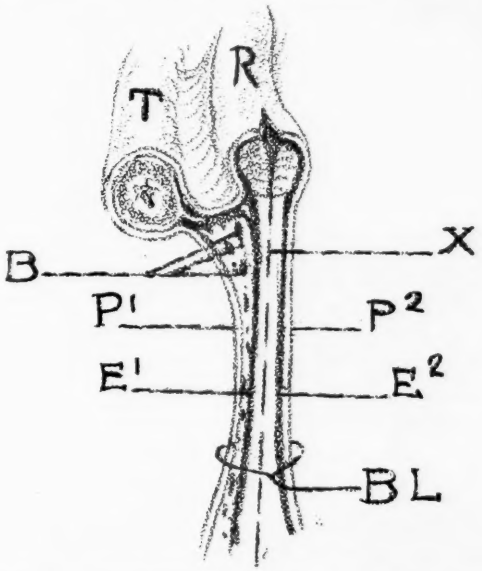


Fig. 3.—Shows a diagrammatic cross section of the tube (*T*), round ligament (*R*), and the broad ligaments (*B.L.*). The broad ligament (*B.L.*) is composed of four distinct layers of tissue, namely, two layers of peritoneum (P^1, and P^2) and two layers of endopelvic fascia (E^1 and E^2). The main blood vessels of the broad ligaments (*B*) are between the upper layer of peritoneum (P^1) and the upper layer of endopelvic fascia (E^1). A longitudinal incision through the center of the round ligaments (*R*) leads directly into an avascular space between the two layers of endopelvic fascia (E^1 and E^2) as represented by the dotted line *X*.

quent pregnancies, he was convinced that the operation that had been devised was a marked improvement over procedures which utilized only the round ligaments to cure retrodisplacements of the uterus.

In 1927, Hurd[5] reported on the end results of 1,000 retroversion operations that had been done by various methods at the Woman's Hospital and found that the Bissell operation had an incidence of recurrence of 1.8 per cent, the lowest for any operation which had been done during the period of time covered by his study.

The Bissell technique for the cure of retroversion has never received the attention which it deserves. The underlying surgical principle of the operation seems to be correct and in keeping with our modern conception of the function of the anatomic structures which support the

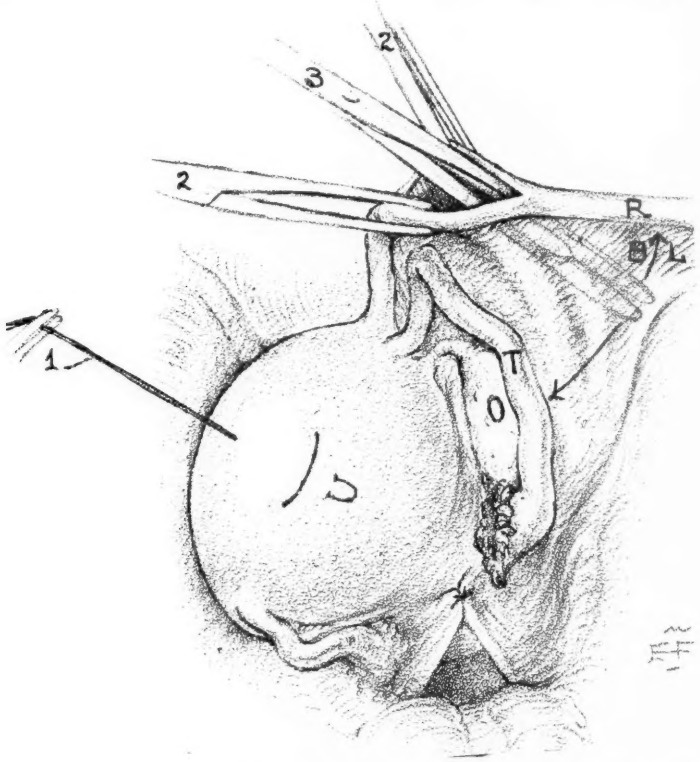


Fig. 4.—Shows the uterus (*U*) being drawn to the left by traction suture (*1*). The distal end of the round ligament (*R*), and broad ligament (*B.L.*) are being held under tension by two Allis clamps (*2*) placed on the margins of the incision made through the round ligament (*R*) as shown in Fig. 2. The avascular space between the two layers of endopelvic fascia (E^1 and E^2), as shown in Fig. 3 is being opened by blunt dissection by means of a Sims artery clamp (*3*). The space is widely opened upward to the round ligament, outward to the lateral wall of the pelvis, and downward to the region of the cardinal ligament.

uterus in a normal anterior position. Certain members of the Woman's Hospital staff have used the operation with so much satisfaction for over twenty years that it seems worth while again to call the attention of gynecologists to this valuable technique and to emphasize the advantages which it appears to have over the round ligament operations that are usually employed for the cure of retroversion.

The various steps in the technique as devised by Bissell are shown in Figs. 1 to 11.

COMMENT

From a study of the Bissell technique as described above, it is obvious that it requires painstaking dissection and careful reconstruction of the relaxed ligaments. However, the planes of cleavage are practically bloodless and the dissection can be easily and quickly carried out by any experienced surgeon.

The advantages of the operation are that:

1. Normal physiologic function of the relaxed round and broad ligaments is restored so that the uterus is supported as nature apparently intended it to be.

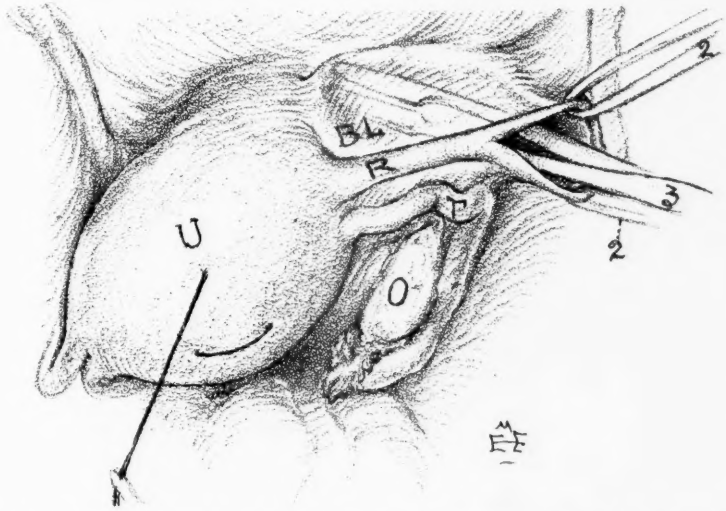


Fig. 5.—Shows the mesial ends of the round ligament (*R*) and broad ligament (*B.L.*) being held under tension by two Allis clamps (*2*) to allow completion of the opening of space between the two layers of endopelvic fascia (E^1 and E^2), as shown in Fig. 2, by means of the Sims artery clamp (*3*). At the uterine end of the broad ligament (*B.L.*), the space is opened from the round ligament to the cardinal ligament area at the level of the internal os of the cervix and well up to the lateral margin of the uterus.

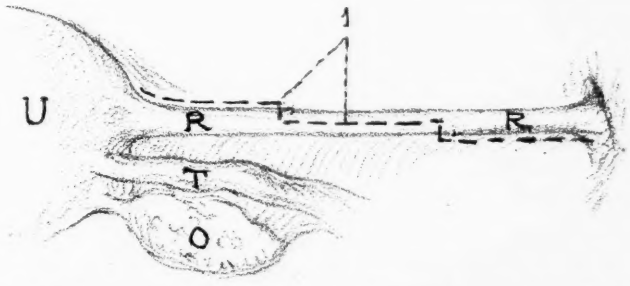


Fig. 6.—After the avascular space between the two layers of endopelvic fascia of the broad ligament has been freely opened as shown in Figs. 4 and 5, the lower layer (peritoneum and endopelvic fascia) is detached from the proximal end of the round ligament (*R*), and the upper layer (peritoneum and fascia) is detached from the distal end of the round ligament (*R*). The dotted line (*1*) shows the line of the longitudinal incision through the center of the middle third of the round ligament (*R*) and indicates the course of incisions used to detach the combined peritoneal and endopelvic fascial layers from the proximal and distal ends of the ligament. The middle third of the round ligament which was split longitudinally at the beginning of the dissection is then excised.

2. The method of shortening the relaxed upper layers of the broad ligaments tends to shift the structures which support the uterine adnexa toward the lateral walls of the pelvis, thereby effectively restoring normal position of the tubes and ovaries which are usually prolapsed when the uterus is retroverted.

3. Painful areas about the points of fixation of the round ligaments to the anterior abdominal wall are avoided.

4. Conditions for subsequent pregnancies are the same as though an operation for retroversion had never been done. In other words normal anatomic relationship of the pelvic organs and their supporting structures is restored without any change in the mechanical principles involved.

The disadvantage of the operation is that the technique is more time consuming and requires more surgical skill than the usual round ligament operations. Because the procedure requires more time, it may

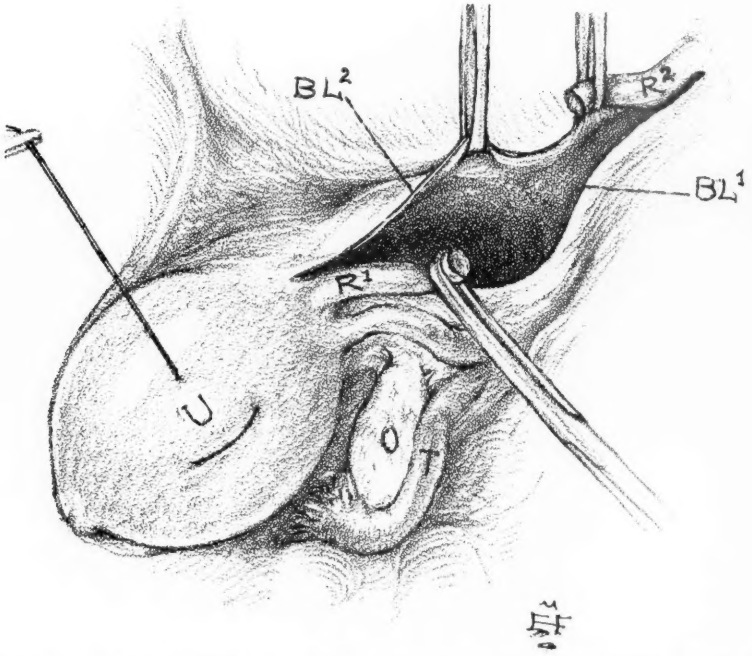
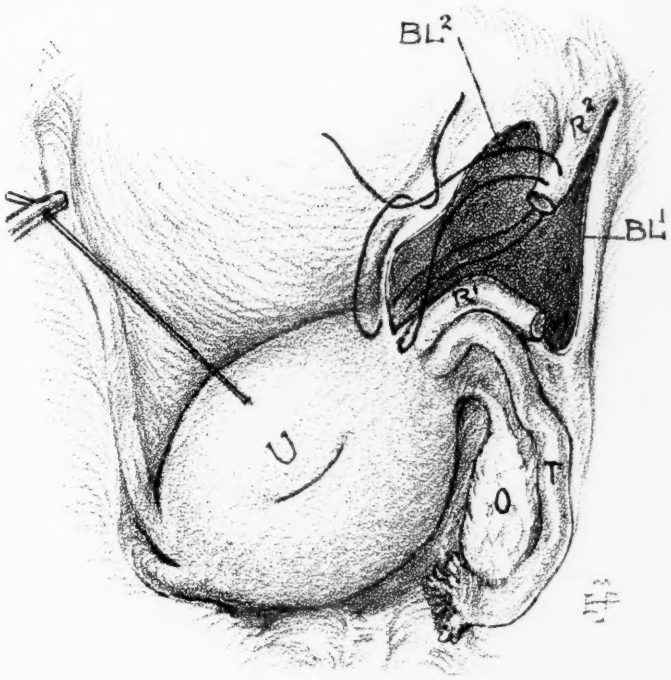


Fig. 7.—Shows the completed dissection. The upper and lower layers of the broad ligament (*B.L.*¹ and *B.L.*²) are being retracted to demonstrate the avascular space between the two layers of endopelvic fascia in the broad ligament. The middle third of the round ligament has been excised. The upper layer of the broad ligament (*B.L.*¹) has been detached from the upper border of the distal one-third of the round ligament (*R*²) and the lower layer of the board ligament (*B.L.*²) has been detached from the proximal one-third of the round ligament (*R*¹).

be unwise to combine it with an extensive vaginal plastic operation to repair birth injuries. It is our practice to adopt some simpler type of procedure when retroversion is complicated with adnexal inflammatory disease to avoid possible increased surgical risk as a result of extensive dissection of the broad ligaments.

Data regarding 376 operations for retroversion by the Bissell technique, performed from 1918 to 1939 inclusive, are recorded in Tables I to VII. The operations were performed by 21 members of the surgical staff.



Figs. 8, 9, 10, and 11.—Show various steps in the reconstruction of the round and broad ligaments.

Fig. 8.—Shows the proximal end of the distal fragment of the round ligament (R^2) being sutured with linen into the denuded angle at the junction between the uterus (U) and proximal fragment of the round ligament (R^1).

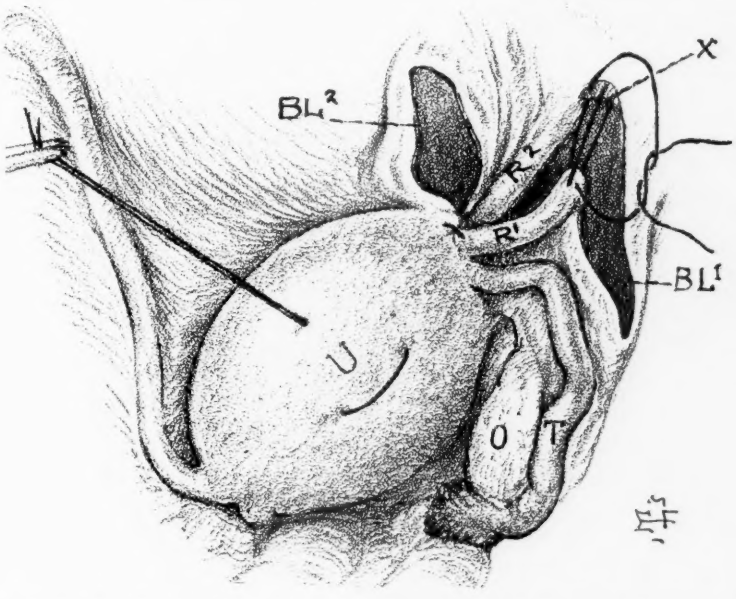


Fig. 9.—Shows the distal end of the proximal fragment of the round ligament (R^1) being sutured with linen to the fascial margin of the internal inguinal ring X.

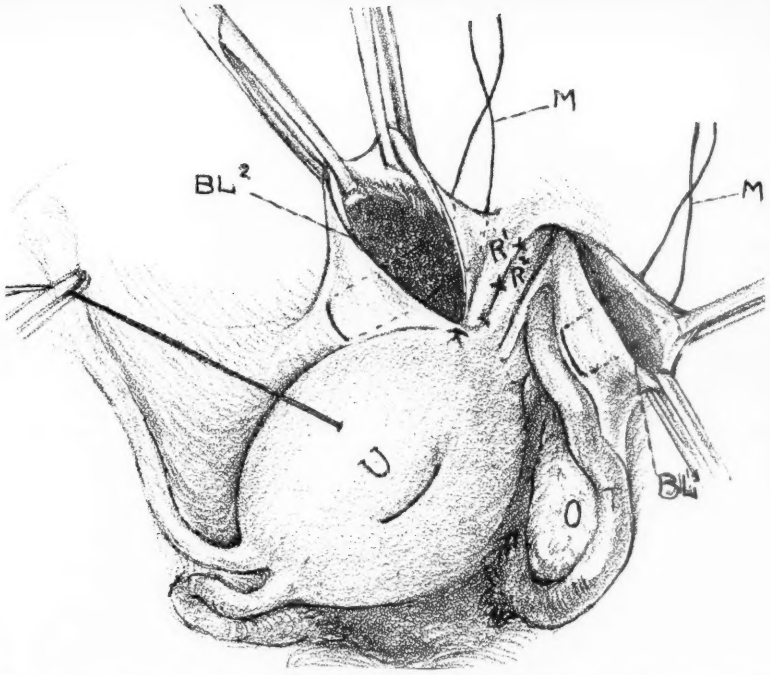


Fig. 10.—Shows the two portions of the round ligaments (R^1 and R^2) united to each other with interrupted sutures of chromic catgut No. 1. After the round ligament (R^1 and R^2) has been reconstructed it will be noted that both layers of the broad ligament are much relaxed, leaving a fold of the lower layer of the broad ligament ($B.L.^2$) near the uterus and a fold of the upper layer ($B.L.^1$) near the lateral wall of the pelvis. The relaxation in both these folds is taken up with mattress sutures (*3*) of chromic catgut No. 1.

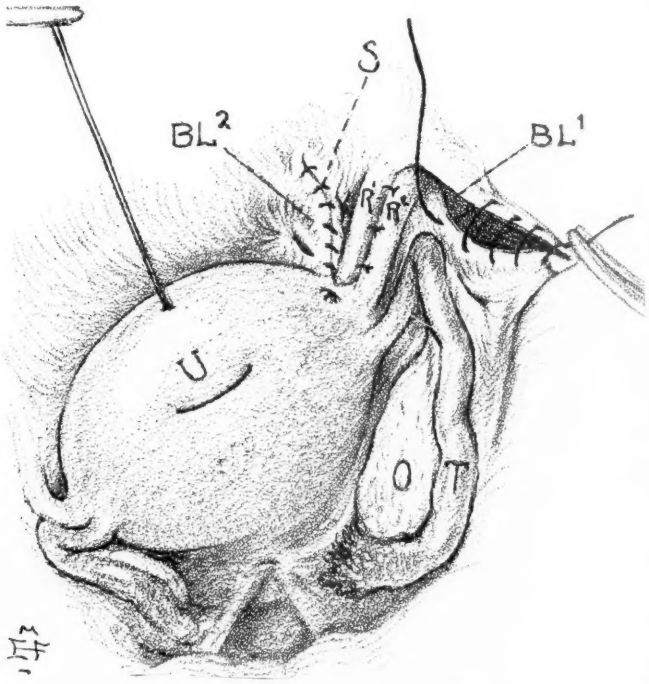


Fig. 11.—Shows the upper margins of each of these folds composed of peritoneum and one layer of endopelvic fascia whipped over with running sutures (*S*) of chromic catgut No. 1, thereby completing the reconstruction of the ligaments.

Table I shows the high incidence of patients that were operated upon within the childbearing period.

TABLE I. DISTRIBUTION OF 376 CASES AS REGARDS, COLOR, MARITAL STATUS AND AGE

		AGE INCIDENCE	
Hospital Status:		YEARS	NUMBER
Private patients	167	Up to 20	16
Ward patients	209	20 to 25	91
Color:		25 to 30	129
White	336	30 to 35	84
Colored	40	35 to 40	38
Marital Status:		40 to 45	10
Single	61	No record	8
Married	315	Total	376

TABLE II. RECORD OF PREGNANCIES IN THE 376 PATIENTS PREVIOUS TO OPERATION

115 patients had never been pregnant.	
95 patients had had 151 *spontaneous abortions.*	
23 patients had had 45 *induced abortions.*	
219 patients had had 426 *term pregnancies.*	
Total No. of pregnancies 622.	

Although 376 of the patients had had 622 pregnancies, many either complained of sterility or wished subsequent pregnancies.

TABLE III. SUMMARY OF CHIEF PREOPERATIVE COMPLAINTS IN THE 376 CASES

		TOTAL
1. Pain:		234
Lower abdomen and pelvis	135	
Backache	97	
Rectal	2	
	234	
2. Menstrual Disorders:		72
Dysmenorrhea	31	
Menorrhagia	20	
Metrorrhagia	15	
Irregular menses	5	
Amenorrhea	1	
	72	
3. Sterility	16	16
4. Leucorrhea	15	15
5. Vaginal protrusion (birth injuries)	12	12
6. Miscellaneous	20	20
7. No record	7	7
		376

In taking histories, it is the routine custom at the Woman's Hospital to record physical complaints in the order of their importance in the minds of the patients. Table III is a summary of the chief complaints as recorded on the 376 case histories reviewed for this study.

Table IV shows the type and number of abdominal and vaginal operations that were done in addition to the 376 operations for retroversions. The uterosacral ligaments were shortened in only 8 cases. Although the principle involved in this step in technique appears to be correct, it is obvious that good results can be achieved without it.

Follow-up records were available in only 255, or 67.8 per cent, of the 376 patients operated upon. Difficulties in getting satisfactory follow-up records were increased

TABLE IV. SUMMARY OF OPERATIVE PROCEDURES IN 376 CASES

Abdominal Operations:	
Operation for retroversion, Bissell technique	353
Operation for retroversion, modified Bissell technique	23
Operation for uterine adnexal disease	95
Separation of peritoneal adhesions	71
Shortening uterosacral ligaments	8
Appendectomy	289
Myomectomy	24
Vaginal Operations:	
Uterine curettage	134
Cauterization of cervix	38
Plastic operations on cervix	42
Plastic operations on vagina and cervix	14
Plastic operations on vagina	20
Hernia (inguinal 1, ventral 1, femoral 2)	4
Hemorrhoids	1

by the fact that 44.4 per cent of the 376 operations were performed by members of the staff upon their private patients. Table V is a summary of the varying periods of time during which 255 patients in the series were followed.

Table VI is a summary of the known facts regarding the pregnancies which occurred following operation in the 255 patients who were followed.

TABLE V. DURATION OF FOLLOW-UP OF 376 PATIENTS

MONTHS	NO. OF PATIENTS
1 to 6	34
6 to 12	49
12 to 18	41
18 to 24	54
Over 24	47
Over 36	52
Never examined	99
Total	376

TABLE VI. SUMMARY OF PREGNANCIES IN 255 PATIENTS FOLLOWED AFTER OPERATION

64 women had 73 pregnancies with the following outcome:	
Spontaneous abortion	19
Induced abortion	2
Therapeutic abortion (Cardiovascular disease)	1
Delivered at term	39
Pregnant when last examined	12
Total	73

TABLE VII. SUMMARY OF FAILURES FOLLOWING OPERATION FOR RETROVERSION IN 376 CASES

OPERATION	NO. OF OPERATIONS	NO. FOLLOWED AFTER OPERATION	NO. OF FAILURES	INCIDENCE OF FAILURE PER CENT
Bissell Standard technique	353	255	5	1.9
Bissell Modified technique	23	22	1	4.5
Total	376	277	6	2.1

When unsatisfactory results occur following the Bissell operation, it is the conviction of surgeons who have used the technique that they are

due to undercorrection of the attenuated ligaments at time of operation rather than to their subsequent relaxation.

The following is a summary of the records of the 6 cases in which operations for retroversion by the Bissell or modified Bissell techniques failed.

1. Mrs. McD. (22490), aged 28 years, white, nulliparous. Chief complaint: irregular excessive periods. Operation: Uterine curettage, Bissell operation for retroversion, separation of peritoneal adhesions, appendectomy, and femoral hernoplasty. Observed for four months after operation. Uterus retroverted second degree at last visit.

2. Mrs. B. (40393), aged 26 years, white, had had one induced abortion and one term pregnancy. Chief complaint: Pelvic pain. Operation: Retroversion (modified Bissell). History of acute pelvic inflammatory disease within six months after operation. Term pregnancy starting sixteen months after operation. Observed for eighteen months. Uterus completely retroverted after pregnancy.

3. Mrs. W. (34020), aged 25 years, colored, had had one term pregnancy. Chief complaints: Irregular menses and pelvic pain. Operation: Uterine curettage, retroversion (Bissell), appendectomy. Difficult term delivery in another hospital one year after operation. Observed thirty-seven months. Uterus retroverted second degree.

4. Mrs. H. (34324), aged 21 years, white, had had one spontaneous abortion. Syphilis at nineteen years. Chief complaints: Pelvic pain and dyspareunia. Operation: Retroversion (Bissell), appendectomy, separation of adhesions. Delivery one year after operation by difficult medium forceps; baby was eleven days postmature. Weight of baby 8 pounds 12 ounces. Observed for eighteen months after operation. Uterus was completely retroverted.

5. Mrs. P. (34722), aged 27 years, white, nulliparous. Chief complaint: Metrorrhagia. Operations: Retroversion (Bissell), separation of adhesions. Treated in clinic for acute pelvic inflammatory disease within six months after operation. Observed for thirty-seven months. Uterus completely retroverted.

6. Mrs. C. (32262), aged 28 years, white, had had 2 spontaneous abortions and 2 term pregnancies. Had been treated for syphilis. Previous appendectomy. Chief complaints: Backache and pelvic pain. Operations: Trachelorrhaphy, repair of laceration pelvic floor, retroversion (Bissell), separation of adhesions. Discharged from follow-up in 1925, twenty-eight months after operation. Uterus completely retroverted. Readmitted fifteen years later for operation for chronic adnexal disease and fibroids.

In the above case histories it will be noted that follow-up records showed that of the 6 failures, 5 were after the standard Bissell technique and one after a modified Bissell technique. Factors contributing to the failures may have been acute pelvic inflammatory disease within six months after operation in 2 cases; a modified Bissell technique in 1 case; pregnancy and delivery within one year in 1 case, and pregnancy and difficult medium forceps delivery of an 8 pound 12 ounce postmature baby in 1 case.

The Bissell technique requires more surgical skill than the usual round ligament types of operations. Four of the 6 failures occurred in patients operated upon by resident surgeons under supervision.

SUMMARY

To summarize some of the facts regarding retroversion, and the relationship of retroversion and its associated conditions to pregnancy, it may be stated that:

1. These conditions are not infrequently the cause of sterility, early abortion, and unpleasant symptoms following abortion and delivery.

2. Unless it is known that retroversion preceded pregnancy, postabortal and post-partum retroversion should be treated by palliative means to reduce the incidence of permanent retrodisplacements of the uterus.

3. Selection of cases for treatment by surgical means should be based on painstaking physical examinations and therapeutic tests to be sure that preoperative pelvic symptoms are gynecologic in origin.

4. Associated functional and pathologic conditions of the uterine adnexa more frequently constitute indications for operation than retrodisplacement of the uterus.

5. Operations for the cure of retroversion and its associated conditions should usually be aimed at preserving the child-bearing function and establishing anatomic and physiologic conditions which will be favorable for subsequent pregnancies.

6. Retroversion of the uterus is caused by relaxation of the broad as well as the round ligaments.

7. Operations for the cure of retrodisplacements of the uterus should be done by techniques which restore the function of the broad as well as the round ligaments.

8. The incidence of failure in operations for retroversion could probably be reduced if conception could be postponed until at least six months after operation.

REFERENCES

(1) *Rubin, I. C.:* Obstetrics and Gynecology, 3: Philadelphia and London, 1933, W. B. Saunders Co., p. 173. (2) *Findley, W. M.:* Am. J. Obst. & Gynec. **24:** 874, 1933. (3) *Crossen and Crossen:* Operative Gynecology, St. Louis, 1938, The C. V. Mosby Co., p. 353. (4) *Bissell, Dougall:* Am. J. Obst. **74:** 1, 1916. (5) *Hurd, R. A.:* Am. J. Obst. & Gynec. **13:** 742, 1927.

33 East 68 Street

DISCUSSION

DR. JOSEPH L. BAER.—This eloquent plea for the survival and wider recognition of the Bissell operation for retrodisplacement is worthy of the best traditions of a great hospital. The speaker showed magnificent results for this operation.

I am in complete accord with much that the essayist has said. However, I am in complete and fundamental disagreement with him on the role of the round ligaments. I believe they play no part in the establishment and maintenance of antedisplacement of the uterus. Therefore, I believe they have nothing to do with the development of retrodisplacement. They have one obvious function. They are massive guy ropes which help to fix the fundus uteri when the uterus goes into labor. Palpation of the abdomens of women in labor frequently reveals on one and sometimes both sides a remarkable hypertrophy of the round ligaments. If the patient has an obstruction, the obvious role of these round ligaments must be clear. They are fixation points for the fundus uteri when the organ is in labor. Inspect the pelvis in a nullipara in whom there is normal anteflexion. As one looks in from the open abdomen the round ligaments can be seen describing an enormous arc from the cornua to the internal inguinal ring, underlying the anterior peritoneum of the broad ligaments, completely relaxed and much longer than the distance between the cornu and the ring on the same side. Displace that fundus backward into the cul-de-sac as far as you please and you will see that the round ligaments do not become taut. How can such structures be given credit for the maintenance of normal anteplacement of the uterus? The erect posture and the consequent rotation of the pelvic girdle as the infant child begins to walk, the growth and descent of the uterus into the true pelvis with adolescence, these, I believe, are the steps which result in pressure

against the posterior surface of the uterus, thus turning, bending and holding it forward against the bladder and symphysis. The 20 per cent of normal nulliparas who have retrodisplacement without symptoms have it either as a result of failure of this rotation mechanism or defective development of the genitalia themselves.

So long as normal development takes place in the infant girl who has normal genitalia, there is also normal antedisplacement of the uterus, not by virtue of the round ligaments but by virtue of the play of intra-abdominal forces. The corpus uteri, freely movable, riding on a flexible joint, is forced forward; it stays there as long as the parametrium and paracolpium remain adequate and the space between the bladder and the uterus remains free of bowel.

How then do we explain the splendid results shown in this paper? The essayist has pointed out that the feature which distinguishes the Bissell operation from other round ligament shortening methods and gives it added merit, is the puckering of the underlying broad ligament structures. Here we are dealing with peritoneal folds overlying the thinnest possible areolar tissue. I cannot believe that that is the answer for the success which has been attained with the Bissell procedure. This operation succeeds because it utilizes available structures to pull the fundus forward. This keeps the bowel out of the vesico-uterine angle and exposes the dorsum of the uterus to the sustaining effect of intra-abdominal pressure. Its grave disadvantage compared with the other round ligament shortening operations is the time it must consume.

I am convinced that the four types of retrodisplacement which were described, namely, those developmental in origin, those following the trauma of childbirth, those following adnexal and other inflammatory diseases of the pelvic cellular tissue, and the acute traumatic type, should each be treated differently if they require treatment at all. Certainly we today do very many less operations for retrodisplacement than we did twenty years ago. We are much more conservative, and we do a much better job of attempting to treat the real pathology. Only if we can convince ourselves that the retrodisplacement causes symptoms do we proceed to surgery for its correction.

Retrodisplacement following the trauma of childbirth is primarily due to injuries of the superior fascial plane which is the true support of the uterus. As was accurately pointed out by Dr. Aldridge, we have the cardinal ligaments laterally, the pubovesical fascia anteriorly, and the uterosacral ligaments posteriorly. Injury to some of these fascial structures results in a sagging of the uterus. The intestinal coils enter the vesicouterine space anteriorly and the intra-abdominal force does the rest. Surgical cure here is complete reconstruction of the fascial planes, that is by parametrial fixation plus whatever else need be done in the reconstruction of the birth canal.

Retrodisplacement caused by adnexal disease requires abdominal approach, a round ligament shortening with bladder advancement. Uterosacral plication is logical and reliable. The Gilliam suspension operation is entirely dependable if one knows how to carry it out. It will allow for childbirth if the attachment is kept sufficiently away from the symphysis, and the risks of intestinal obstruction are avoided if the attachment is snug.

The women who have normal retrodisplacement without symptoms require no treatment. The acute traumatic type of retrodisplacement requires only immediate replacement and adequate rest to establish a complete recovery.

In the decade from 1920 to 1930, there were 337 operations for retrodisplacements done by the Gynecological Staff of Michael Reese Hospital. Of these, 239 were primary and 98 were secondary to other pathology. In the decade from 1930 to 1940, there were 358 operations for retrodisplacements, of which 230 were primary and but 28 secondary. In the first decade, from 1920 to 1930, the Gilliam suspension operation was the operation of choice, while in the second decade parametrial fixation was done largely. In both decades many other procedures were used. In the total of 695 operations, there were 5 known failures, 2 Baldy-Webster, 2 ventral fixation, and 1 Barrett operation. This is only a slightly higher percentage than the essayist reported for the Bissell operation.

DR. N. S. HEANEY.—I would like to discuss the role of retroversion of the uterus in the production of the symptoms usually attributed to it. In my opinion the

symptoms are not due to the retroversion ordinarily but to the accompanying pathology. The backaches associated with retroversion usually clear up when the accompanying erosion or endocervicitis has been cured. The dysmenorrhea of retroversion also clears up when the cervical pathology, be it an erosion, endocervicitis, or stricture of the cervix, has been done away with, as well as the menorrhagia. At the Presbyterian Hospital last year only seventeen patients were operated upon "for retroversion." Upon a stricter analysis, however, I am quite certain that in most cases the retroversion was not the reason for the operation but was a condition which accompanied the pathology necessitating the operation, such as endometriosis, ovarian cyst, infected appendages, etc. As my experience in gynecology increases the importance of retroversion as a clinical important condition decreases.

DR. ALDRIDGE (closing).—In the discussion Dr. Baer has stated his conviction that the round ligaments have nothing to do with supporting the uterus in an anterior position. He has also reviewed certain theories as to conditions which may cause retroversion. They should be regarded as no more than theories because the exact cause of retroversion has not been established.

In presenting the results of our experience with the Bissell operation, the statement was made that the uterus is held in an anterior position by the normal function of the round and broad ligaments. Regardless of whether this statement is accepted, we are convinced that combined reconstruction of the round and broad ligaments by the Bissell technique, gives us a higher incidence of satisfactory end results in the surgical cure of retroversion than with any other procedure which we use. Furthermore, in a limited series of cases, we have been impressed with the success of the operation in withstanding the strain of subsequent pregnancies.

Dr. Baer favors parametrial fixation, a procedure developed for the cure of prolapse, as the operation of choice to cure acquired retroversion. Although uterine retroversion and uterine prolapse often occur together in the same patient, from the etiologic standpoint we regard the two conditions as distinct clinical entities. We consider the principle involved in parametrial fixation anatomically correct for the cure of prolapse but not for the cure of retroversion. We have no more confidence in parametrial fixation for the cure of retroversion than we have in retroversion operations for the cure of uterine prolapse.

Dr. Heaney has emphasized the importance of associated pathologic pelvic conditions in the causation of symptoms often attributed to the retroversion itself. He believes that if cervical erosion and infection are eradicated, a retroverted uterus will usually assume a normal anterior position. There is evidence to suggest that cervical infections may result in some loss of tone of the structures that support the uterus. However, in our experience, spontaneous cure of retroversion, following successful treatment of cervical infections, is so rare that it cannot be looked upon as a reliable method of treatment for chronic retrodisplacement of the uterus.

Essenberg, Schwind, and Patras: The Effects of Nicotine and Cigarette Smoke on Pregnant Albino Rats and Their Offspring, J. Lab. & Clin. Med. 25: 708, 1940.

Among others the following results were obtained in a study of a large number of nicotine-injected and smoked female rats and their offsprings: Two-thirds of all the young of treated mothers were underweight and remained so for some time. Of the females injected with nicotine, 63 per cent lost one or more, and 33.3 per cent all of their young. In those exposed to tobacco smoke, these percentage figures were 28 and 13.5, respectively. In both groups, temporary sterility, resorption of young in utero, and abortions were noted.

The writers' final conclusion is: A marked parallelism exists between treated rat females and their young, and human mothers and their young in cases where the mother is a heavy smoker or is employed in the tobacco industry.

HUGO EHRENFEST.

A METHOD FOR EVALUATING THE STRESS OF URINARY INCONTINENCE

ALLAN C. BARNES, M.D., ANN ARBOR, MICH.

(From the Department of Obstetrics and Gynecology, University of Michigan Hospital)

THE importance of the problem of stress urinary incontinence in women is well recognized. The complaint is highly embarrassing or even incapacitating to the patient; it is met with frequently and its cure is difficult. The sizable literature which has appeared on this topic attests to the fact that this problem is far from settled. Many contributions have added new operations or new operative modifications to the already crowded list of therapeutic measures. However, a survey of some of the reported results of these operative procedures indicates that the percentage of patients cured ranges from 36 to 100 per cent, with an average for any particular procedure close to 80 per cent.[1-9, 13, 23] In general, the number of cures diminishes in direct ratio to the length of time allowed to elapse between operation and the follow-up studies. And the fact that from 6 to 14 per cent of the reported cures have been in patients subjected to repeated operations serves as a further indication that the therapeutic situation in respect to this complaint is not entirely satisfactory.

It has been the opinion in this clinic that a sufficient number of well-established operative procedures are already available for the treatment of incontinent patients. It has been frequently demonstrated that certain of these can give satisfactory results when judiciously chosen and applied with a knowledge of the underlying disturbance of function. Therefore no new surgical procedures are described in this paper. It presents rather a clinical and investigative review of the fundamental factors in the pathologic physiology of stress urinary incontinence, together with a clinical test to serve as an aid in its correct evaluation and the selection of the proper operation.

PHYSIOLOGIC CONSIDERATIONS

In the normal female at rest, the involuntary urethral sphincter will retain urine in the bladder. This principle has been so clearly demonstrated by the excellent work of Denny-Brown and Robertson,[10] that extensive discussion here is not necessary. It is well to bear in mind, however, the nature of involuntary sphincter action. With the bladder at rest the internal sphincter is firmly closed, but it is not in a state of continuous contraction. Involuntary sphincters do not maintain "unmeaning contraction."[11] If from its resting closed state an involuntary sphincter is gradually distended, it will exert a contractive

force proportionate to the degree of distention. If nothing is distending it, the sphincter does not contract, but once it has been opened by trigonal action and stretched by fluid passing through it, the muscle tends to close. Whether this reaction is affected by nervous plexus or is a purely muscular phenomenon remains to be determined, but the loss of this "reactive contraction" mechanism undoubtedly contributes much to disability of the female bladder.

With a cough, sneeze, or other strain which produces a rise in intra-abdominal pressure, the voluntary sphincters are brought into play, and normally these are sufficient to provide the added barrier necessary to resist the associated rise in intracystic pressure.[12] With loss of internal sphincter tone, it is probable that the external voluntary sphincter is sufficient to preserve continence while the patient is quiet.[13] But the normal state of balance is disturbed, and the patient has no additional barrier to employ against the sudden (but not necessarily large) rise of bladder pressure associated with laughing, coughing, or sneezing.

Since urinary incontinence, regardless of exact etiology, represents a momentary increase in the forces of urinary expulsion over the powers of urethral resistance, it would appear that incontinence could result from (a) an increase in urinary expulsive force or intravesical pressure, (b) a lowering of the powers of resistance or urethral sphincter action, or (c) a combination of (a) and (b).

(a) *Increase in Urinary Expulsive Force.*—The partial incontinence which so often develops in the last trimester of pregnancy, and that associated with large pressure-producing pelvic tumors are clear examples of incontinence chiefly on the basis of elevated intravesical pressure. But aside from these, the actual causative relationship between increases of intravesical pressure and diurnal incontinence is difficult to prove.

In an effort to evaluate the rôle played by the forces of expulsion in stress incontinence, we have performed over 80 cystometric studies on 32 patients with some degree of pelvic floor relaxation.[14] Fig. 1 is an illustration of three such curves obtained on the same patient. Curve B is a postoperative study, and represents a normal cystometric reading. Curve C is a preoperative study obtained in the traditional manner, and reveals a bladder of somewhat increased capacity with pressures slightly lower than normal. But the cystometrogram A is also a preoperative study on the same patient, and by comparison with C, this shows a relatively small capacity bladder of higher intravesical pressure. The essential difference in the obtaining of these two readings was that in curve A, the patient's descensus was drawn down to the position it occupied while she was on her feet. In other words, the descensus uteri in this case could produce a relative increase of intravesical pressure while the patient was standing which would not have been indicated by the traditional cystometric reading performed with the patient recumbent.[15] In like manner it can be shown that pressure producing tumors (Fig. 2), and large rectoceles which press against the bladder result in relative rises in intravesical pressure.

We are not suggesting that these conditions are frequent causes of stress urinary incontinence in women. Nevertheless, since the ultimate objective of treatment is to restore a balance in which the powers of urethral resistance are greater than the forces of urinary expulsion, it is well to bear in mind that

intravesical pressures may frequently be elevated, thereby making increased demands on the urethral sphincter mechanism.

(b) *Decrease in Urethral Resistance.*—Damage to the sphincter mechanisms or their supporting structures may lower their efficiency to such an extent that they are unable to preserve continence. While this principle is a generally accepted one, the manner in which damage may occur, and the exact nature of such damage, has not been conclusively demonstrated. Most frequently the trauma of childbirth is assumed to be the chief cause of injury to the mechanism of urinary continence. While it is true that 150 patients with incontinence had a higher average parity than 140 continent parous women of the ward service at the University Hospital (4.8 children apiece compared to 3.6), we have also had two nulliparous patients with stress incontinence, and one of our most severe cases occurred in a para i who had a short easy labor, giving birth to a 5-pound child. The theories concerning the nature of the damage to the urethral sphincters are legion. A complete cataloguing of these theories would be of no value here. Suffice it to say that they all fall principally into two groups: those maintaining the primary damage to be on the

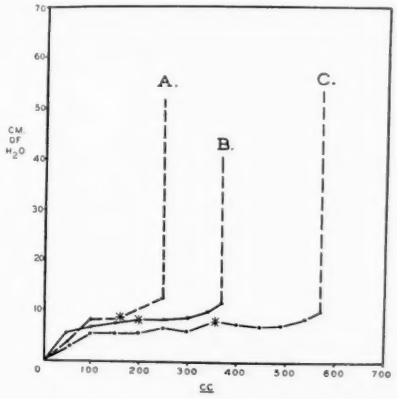


Fig. 1.

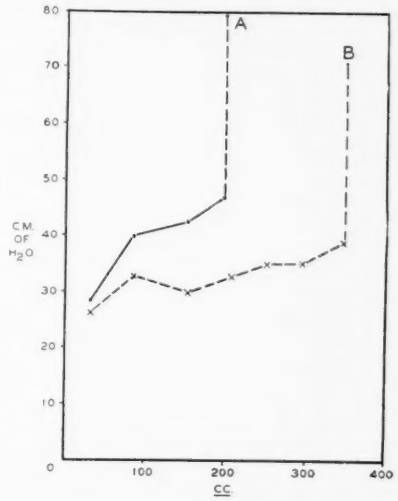


Fig. 2.

Fig. 1.—Three cystometric curves from the same patient (see text).

Fig. 2.—Preoperative (*A*) and postoperative (*B*) curves on patient with bilateral large ovarian fibroma. Cystometrics obtained with patient sitting up.

urethra or its sphincters,[16, 17] and those stating that the essential changes involve peri-urethral or supporting tissues.[18, 19] In all probability the problem is not one of "either . . . or," but of "both . . . and."[20, 21]

The degree of the functional damage may be interpreted from the clinical history obtained. At onset the incontinence often seems to result from a failure on the patient's part to augment her sphincter mechanism rapidly enough. If she sneezes several times in succession, she will be incontinent only with the first sneeze. The reflex muscular tightening which reinforces the sphincter mechanism in the face of increased intra-abdominal pressure is delayed rather than completely lost. Subsequently there may be incontinence associated with all coughing, laughing or other relatively rapid changes in intra-abdominal pressure, while continence is preserved on lifting heavy objects, or in other situations where ample time may be taken to adjust the musculature to the increased strain. Finally there is complete incontinence on all activity or even incontinence while the patient is recumbent.

EVALUATION OF FUNCTIONAL DISABILITY

The accurate diagnostic evaluation of patients with partial urinary incontinence has not in the past been easy. The patient's history and the physical examination do not tell the entire story, for seemingly mild cases will unpredictably resist every form of therapy attempted. More information than the degree of pelvic relaxation, if any, and the patient's description of her symptoms is necessary for the competent selection of the proper operative procedure.

During the past year we have been employing in this clinic a test based on the physiologic principles outlined above, and designed to give additional diagnostic information necessary for the thorough evaluation of these cases. It consists essentially of three studies, all relatively easy to perform.

Fig. 3.—Normal anteroposterior sphinctometric. Balloon shadow obliterated by urethral resistance, leaving balloon dilated only inside internal and outside external meatus.

1. *Measurement of Intravesical Pressure.*—With a standard volume of fluid in the bladder, and with the patient standing, direct manometric readings are obtained.[22] We have optionally selected 3½ ounces of physiologic saline solution, and have determined normal readings on a group of continent patients. For the occasional patient who cannot accommodate 3½ ounces, the bladder is filled to capacity and the reading (usually found to be markedly elevated) is taken. Since most partial incontinence is suffered while the patients are active and on their feet, we feel that the standing position in which this reading is taken provides a more useful comparative figure.

2. *Direct Measurement of Urethral Resistance.*—The method we have adopted for measuring the strength of urethral resistance is a modification of an experiment performed some years ago by Kennedy.[23] A small balloon composed of two superimposed finger cots is inserted in the urethra, filled to a known manometric pressure with a 90 per cent sodium iodide solution, and an x-ray taken. Studies on normal patients indicate that under these conditions the entire urethra should remain closed and obliterate the balloon shadow at a pressure of 35 cm. of fluid, and it is at this pressure that the x-ray is taken. The result in a normal patient is shown in Fig. 3. The bladder is filled with 180 c.c. of an 8 per cent solution of sterile sodium iodide, which is well tolerated, and the balloon is seen to be compressed throughout the length of the effective resistant force of the urethra. The essential point to be observed in this film is whether or not the dilatation of the balloon at its inner end lies

Fig. 4.

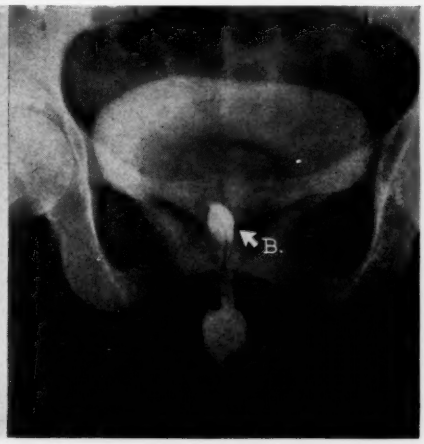


Fig. 5.

Figs. 4 and 5.—Two abnormal anteroposterior sphinctometrics, showing varying degrees of weakness at internal sphincter area. Balloon dilates at inner end before urethrovesical junction is reached (*A* and *B*). Compare with Fig. 3.

within the bladder shadow. In other words, the effective urethral resistant force must reach the urethrovesical junction. Variations from this normal picture occurring in two patients with differing degrees of sphincteric weakening are shown in Figs. 4 and 5.

3. *Indirect Measurement of Internal Sphincter Strength.*—This determination is also made in conjunction with x-ray, the film being taken in the oblique, and an indwelling watch chain used to mark the course of the urethra as suggested by Stevens and Smith[24] (Fig. 6). As this film is exposed, the patient is asked to strain down as hard as she can. With straining intravesical pressures from 60 to 80 cm. of water may be obtained, so that in this study the urethra is subjected to a much greater force than in the first film, but it is a force applied in a more physiologic manner, i.e., from within outward.

In a normal person, a rise in intravesical pressure alone cannot force fluid through the internal sphincter without a detrussor contraction of

the bladder.[10] Hence, in this x-ray the bladder floor should be flat at the urethrovesical junction, and should have the relationship with the urethra of two straight lines to each other. Funneling of the bladder floor toward the urethra indicates that mere increase in intravesical pressure, unassociated with contraction of the trigone, has forced fluid through the internal sphincter, and denotes a weakening of this sphincter.[25] Examples of this situation are shown in Figs. 7 and 8.

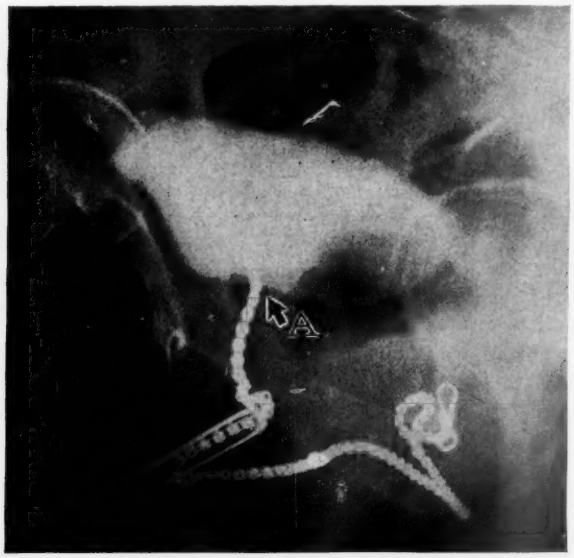


Fig. 6.—Normal oblique view, with watch chain in urethra. Despite the fact that the patient is straining, internal sphincter area (*A*) shows no funneling.

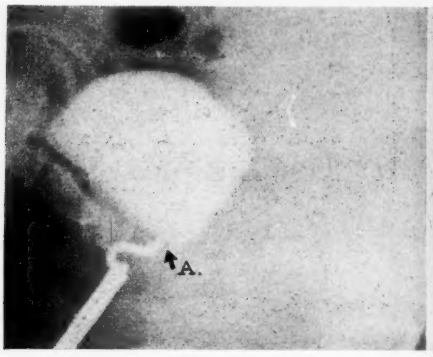


Fig. 7.

Fig. 8.

Figs. 7 and 8.—Two variations from the normal oblique view. Marked relaxation (*A*) and minimal funneling (*B*). See also Fig. 10.

The information obtained from these studies permits a much better understanding of the patient's incontinence. With such information in mind, a complete program for the treatment of partial incontinence in women should include measures designed to (a) lower intracystic pres-

sure where this is found to be increased, and (b) re-establish urethral resistance where this is diminished.

(a) In a patient with pelvic relaxation and descensus, plastic repair will lower the elevated intravesical pressure. Obtaining intravesical pressure readings pre- and postoperatively on 34 patients has shown that procedures which include plaiting of the pubovesicocervical muscle layer, correction of rectoceles, or operations for the removal of large uterine or ovarian tumors accomplish this result.

Fig. 9.—Preoperative (left) and postoperative (right) sphinctometric. Minimal relaxation indicated by dilatation of balloon at *A* outside bladder. Following Kelly stitch this is corrected (*B*).

Fig. 10. Fig. 11.

Figs. 10 and 11.—Minimal funneling at *A* preoperatively. Bladder floor flat at *B* following Kelly stitch.

While causative relationship between increased forces of expulsion and stress incontinence cannot be completely demonstrated and is not here claimed, every gynecologist has encountered cases of incontinence cured by nothing other than plastic repair, and the associated reduction in intravesical pressure may well be the explanation. Certainly it is asking much of a purely local procedure such as fulguration of the internal sphincter area, the Kelly stitch, or the "direct muscle plastic" of Stoeckel[17] to retain urine which may be at pressures 30 per cent above normal.

(b) The re-establishment of functional urethral resistance has often been lost from view in attempts to re-establish urethral anatomy. Some writers have claimed a constant relationship between incontinence and changes in anatomic

structure: d'Azevedo and Campos[26] (loss of angle of urethra to bladder floor), Taylor and Watt[27] (descent of posterior urethral wall), and Thomsen[28] (loss of anterior angulation of urethra). Our x-rays have not confirmed a constant association of these factors with incontinence, whereas continent patients have demonstrated wide variation in urethral angulation. To the patient, function rather than shape is important; a single band able to resist pressure is more valuable than a normally shaped urethra with no inherent power of effective resistance.

Fig. 12. Fig. 13.

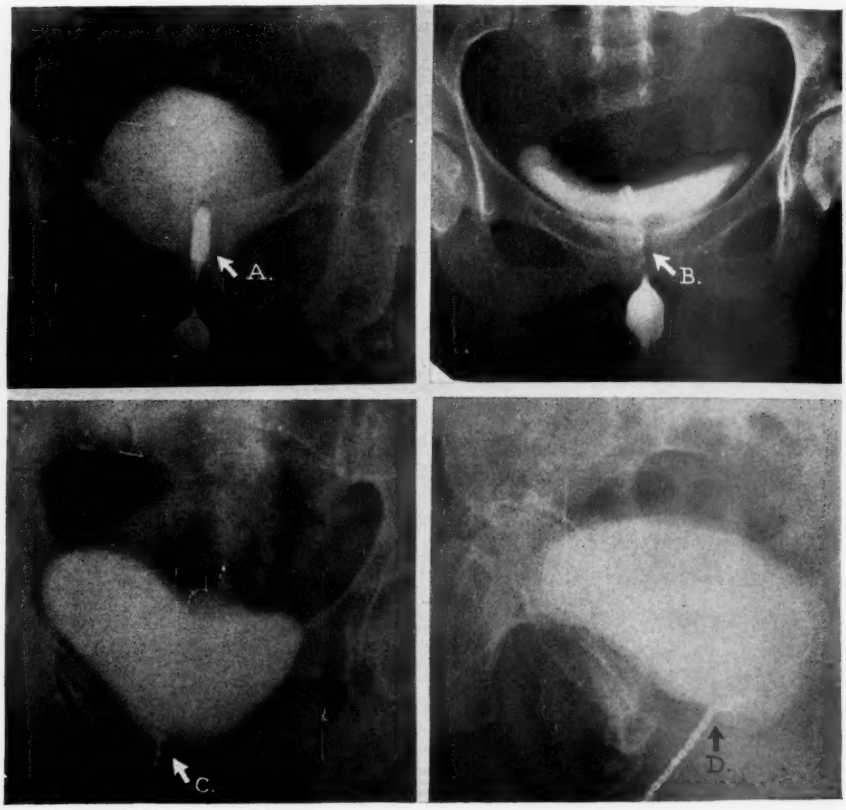


Fig. 14. Fig. 15.

Figs. 12 to 15.—Urethral resistance fails, as shown at *A*, outside bladder. Postoperatively internal sphincter area (*B*) resists pressure satisfactorily. Funneling (*C*) at internal sphincter area corrected by plastic, restoring bladder floor and sphincteric resistance (*D*). Compare postoperative view (Fig. 15) with normal (Fig. 6).

The same type of x-ray studies used in the preoperative evaluation of the patient's disability give a postoperative indication of whether or not effective urethral resistance has been restored. Fig. 9 is the pre- and postoperative anteroposterior view of a patient who had a Kelly stitch type of operation. In the view on the left, the dilatation of the inner end of the balloon can be seen to begin just outside the bladder. Postoperatively, as shown in the film on the right, the urethral ability to contract extends, as it should normally, all the way to the urethrovesical junction. Figs. 10 and 11 are oblique studies before and after simple Kelly stitch. The funneling at the urethral vesical neck is minimal, but postoperatively it is obliterated, and the patient is continent.

In like manner, Figs. 12 to 15 give the preoperative (to the left) and postoperative studies of a patient who was a candidate for a plastic operation. The

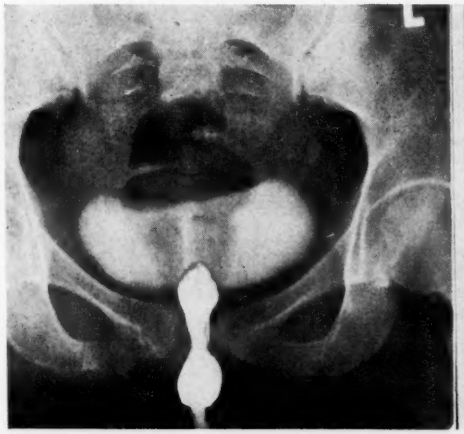


Fig. 16.

Fig. 17.

Fig. 18.

Fig. 16.—Preoperative view (compare with Fig. 3).

Fig. 17.—Postoperative x-ray, with patient relaxed, shows marked improvement.

Fig. 18.—Postoperative x-ray (with pyramidalis tightened) shows sphincteric action of transplant by increased obliteration of balloon shadow. (See text.)

anteroposterior film reveals dilatation for a greater area down the urethra; the oblique view demonstrates more marked funneling and the descent of the bladder floor. Postoperatively, these are corrected in a satisfactory manner by plastic repair, with particular care being taken of the internal sphincter area.

Fig. 16 reveals the type of urethra which has no inherent resistance whatever. Local tightening procedures are of no avail in the face of such complete lack of urethral resistance. Whatever the particular operation selected, it must be one which brings the motive force to the urethra from elsewhere, and this study, therefore, indicates the necessity for some type of transplant operation. This particular patient had a pyramidalis muscle-fascial transplant operation as described by Norman F. Miller,[29] and the postoperative films reveal the result. The film shown in Fig. 17 is in marked contrast to the preoperative film, and shows almost complete closure of the urethra. The next x-ray (Fig. 18) was taken immediately after the film shown in Fig. 17, but as this was exposed the patient was asked to raise her head and shoulders from the x-ray table. This action tightened the rectus and pyramidalis muscles, drew tight the fascial sling under the urethra, and the fact that the patient's postoperative continence was based on a new sphincteric action is clearly demonstrated. It should perhaps be re-emphasized that these x-rays are not primarily pictures of structure, but indicate functional ability to resist force applied against the sphincters.

SUMMARY

The difficulty of the accurate evaluation of stress urinary incontinence and the selection of the correct type of operative procedure for any given case is appreciated by all gynecologists. The principles which form the basis for the treatment of this complaint are here presented, and a clinical test is reported which has been used and found satisfactory as indicating the etiology, the operation of choice, and the results of operation for incontinence. It should be emphasized that this test is not intended to replace, but rather to complement, other methods now in use for the evaluation of partial or stress urinary incontinence in women.

REFERENCES

(1) *Bertone, Carlo:* Riforma med. **52:** 973, 1936. (2) *Douglass, Marion:* Am. J. Obst. & Gynec. **31:** 268, 1936. (3) *Davies, J. W.:* Surg. Gynec. Obst. **67:** 273, 1938. (4) *Frigyesi, Josef:* Arch. f. Gynäk. **160:** 176, 1935. (5) *Gomez, Carlos:* J. d'urol. **45:** 344, 1938. (6) *Lowsley, O. S.:* J. Urol. **36:** 400, 1936. (7) *Millin, T.:* Proc. Royal Soc. Med. **32:** 777, 1939. (8) *Muret, M., and Chapin, O. J.:* Gynec. et obst. **36:** 81, 1937. (9) *Schrattenbach, V.:* Zentralbl. f. Gynäk. **61:** 1848, 1937. (10) *Denny-Brown, D. E., and Robertson, E. G.:* Brain **56:** 149, 1933. (11) *Denny-Brown, D. E.:* New England J. Med. **215:** 647, 1936. (12) *Davids, A. M., Newman, H. F., and Rubin, I. C.:* J. Mt. Sinai Hosp. **4:** 861, 1938. (13) *Young, H.:* Quoted by Davids, Newman and Rubin. (14) *Rose, D. K.:* J. Urol. **40:** 248, 1938. (15) *Idem:* Ibid. **27:** 207, 1932. (16) *Johnston, H.:* Surg. Gynec. Obst. **53:** 96, 1931. (17) *Stoeckel, W.:* Zentralbl. f. Gynäk. **61:** 1224, 1937. (18) *Kennedy, W. T.:* Am. J. Obst. & Gynec. **34:** 576, 1937. (19) *Watson, B. P.:* Brit. M. J. **2:** 566, 1929. (20) *Thomsen, E.:* Acta radiol. **13:** 433, 1932. (21) *Natvig, H.:* Norsk mag. f. laegevidensk. **92:** 325, 1931. (22) *Schwartz, O.:* Handbuch der Urologie, Berlin, 1926. (23) *Kennedy, W. T.:* Am. J. Obst. & Gynec. **33:** 19, 1937. (24) *Stevens, W. E., and Smith, S. P.:* J. Urol. **37:** 194, 1937. (25) *Miller, J. D.:* Ibid. **40:** 612, 1938. (26) *D'Azevedo and Campos:* Quoted by Stevens and Smith. (27) *Taylor, H., and Watt, C.:* Surg. Gynec. Obst. **24:** 296, 1917. (28) *Thomsen, E.:* Acta radiol. **11:** 527, 1930. (29) *Miller, Norman F.:* J. A. M. A. **98:** 628, 1932.

UTERINE BLEEDING INDUCED BY PROGESTERONE

During the Normal Menstrual Interval and in Amenorrhea

Bernhard Zondek, M.D., Jerusalem, Samuel Rozin, M.D., and Morton Vesell, M.D., New York, N. Y.

(From the Gynaecological-Obstetrical Department of the Rothschild-Hadassah University Hospital, Jerusalem, and the Endocrine-Clinic of the Beth Israel Hospital, New York)

IN PREVIOUS publications[1] it has been demonstrated that bleeding during the intermenstrual stage can be obtained in the normally menstruating woman by administering 50 mg. of progesterone during the postmenstrual stage, 10 mg. on five successive days. This type of bleeding which occurs from a proliferatively developed mucous membrane (Fig. 1), usually appeared about 60 hours after the last progesterone injection and persisted from three to five days. We termed it "intracyclic bleeding." The patients told us that the general subjective symptoms appearing previous to and during the period of bleeding were much the same as those which occurred from normal menstruation. If, however, progesterone is given during the intermenstrual stage, at a time when the organism has already developed its own corpus luteum, no bleeding occurs. The level of estrone hormone which, under physiologic conditions, is present during the intermenstruum does not prevent the intracyclic bleeding. If, however, additional amounts of estrogenic hormone are given (10 mg. of estradiolbenzoate on four successive days), this will counteract the bleeding effect of progesterone. Pregneninonol per os has the same effect as progesterone parenterally.[2]

After it had been ascertained that intracyclic bleeding taking place from a proliferatively developed mucous membrane could be induced by progesterone, an attempt was made to use this substance in the treatment of amenorrheic women without the preliminary application of estrogens. Seven out of eight cases of secondary amenorrhea, in which bleeding had been absent from four months to three years, have responded to this treatment. However, we have been unsuccessful with this treatment in five cases of primary amenorrhea.[1]

In the following, we desire to report additional experience with progesterone therapy.*

I. Administration of Progesterone over the Entire Cycle

As has been explained above, it is only in certain phases of the cycle that it is possible to induce bleeding with progesterone. If, therefore, a five days' progesterone treatment is begun at the time of follicular rupture no bleeding occurs, since in this case the exogenous administration of corpus luteum hormone coincides with the endogenous production of this factor. The following experiments make it clear that a certain

*Some of the work referred to was done by B. Zondek and M. Vesell in the Beth Israel Hospital in New York.

interval must elapse between the administration of progesterone and its endogenous production. If progesterone administration is begun during the postmenstrual phase and the treatment then carried on without interruption over the whole of the cycle, no intracyclic bleeding will occur, although a total of 95 or even 105 mg. of progesterone are injected into the organism.

CASE 1.—In this patient, aged 20 years, the menstrual period occurred at a twenty-six-day interval, and bleeding usually persisted for three days. There were no abnormal gynecologic findings. From the fourth day after bleeding had ceased, i.e., the seventh day of the cycle, 5 mg. of progesterone were given intramuscularly daily over a period of nineteen days (95 mg. in all). Bleeding appeared on the expected date of menstruation (twenty-sixth day) and persisted for three days.

CASE 2.—The patient, aged 20 years, had always had normal menstrual periods with bleeding of five to seven days' duration. There were normal gynecologic findings. From the tenth day on, the patient was given 5 mg. of progesterone daily, 105 mg. in all. On the thirtieth day, i.e., on the date of the expected normal menstruation, bleeding set in and persisted for six days. Biopsy performed early during the period of bleeding, revealed that the glands of the uterine mucosa were not overdeveloped, although very large amounts of progesterone had been given. The anatomic picture of the mucous membrane suggested the beginning of the menstrual stage.

II. BLEEDING INDUCED IN SECONDARY AMENORRHEA BY PROGESTERONE ALONE

(a) *The Duration of the Period of Progesterone Administration and Its Influence on the Bleeding Effect.*—After it had been ascertained that it was possible, by five days' administration of 10 mg. of progesterone daily, to produce bleeding in secondary amenorrhea, we tried to shorten the period of hormone administration. Two women, who had been amenorrheic for five months and three years, respectively, were each given a single injection of the whole amount of 50 mg. In neither case did bleeding occur. When, however, this dose was given in two portions on two successive days, bleeding took place (Table I). It is worthy of record that in these cases the

TABLE I. FIFTY MG. OF PROGESTERONE GIVEN ON TWO DAYS IN SECONDARY AMENORRHEA

NO.	NAME	AGE	DURATION OF AMENORRHEA	PROGESTERONE (MG.)	INTERVAL BETWEEN LAST INJECTION AND BLEEDING	DURATION OF BLEEDING
1	K.	18	5 mo.	2 x 25 mg. on two days	72 hr.	3 da.
2	F.	22	3 yr.	2 x 25 mg. on two days	100 hr.	4 da.
3	J.	21	6 yr.	2 x 25 mg. on two days	96 hr.	1 da.

interval between the injection of hormone and the occurrence of bleeding was prolonged. If 50 mg. are distributed over 5 injections, given on five successive days, bleeding usually appears sixty to seventy-two hours after the last hormone injection. If it is, however, given in two portions on two successive days, bleeding does not set in before the lapse of seventy-two to one hundred hours.

(b) *Tabulation of the Cases of Amenorrhea Treated by Progesterone Alone.*—Up to the present, 19 cases of secondary amenorrhea have been treated with progesterone alone. The patients' ages were between 17 and 40 years, and amenorrhea had been present for from four months to seven years. In most of the cases the uterus was found to be hypoplastic. Of the 19 cases, bleeding was induced in 17, which means that in 89.4 per cent the treatment was successful (Table II). The absence of

TABLE II. BLEEDING AND SUBSEQUENT SPONTANEOUS BLEEDING AFTER TREATMENT WITH PROGESTERONE IN SECONDARY AMENORRHEA

NO.	NAME	AGE	DURATION OF AMENORRHEA	UTERINE FINDINGS	PROGESTERONE (MG.)	BLEEDING	SUBSEQUENT SPONTANEOUS BLEEDING
1	J.	21	4 mo.	Normal	5 × 10 mg. on 5 days	+	2 spontaneous periods of bleeding, then amenorrheic again
2	S.	23	6 mo.	Normal	5 × 10 mg. on 5 days	+	None
3	H.	32	6 mo.	Normal	5 × 10 mg. on 5 days	+	
4	L.	40	6 mo.	Normal	5 × 10 mg. on 5 days	+	
5	W.	26	9 mo.	Hypoplasia	5 × 10 mg. on 5 days	+	1 period of bleeding, no further observation
6	F.	24	1 yr.	Normal	5 × 10 mg. on 5 days	+	
7	K.B.	19	1 yr.	Hypoplasia	5 × 10 mg. on 5 days	+	None
8	O.	28	1 yr.	Normal	5 × 10 mg. on 5 days	+	1 spontaneous period of bleeding
9	A.	17	1 yr.	Hypoplasia	5 × 10 mg. on 5 days	+	
10	K.	19	14 mo.	Hypoplasia	5 × 10 mg. on 5 days	+	None
11	M.	37	15 mo.	Normal	5 × 10 mg. on 5 days	+	3 spontaneous periods of bleeding, reports pregnancy
12	D.	19	18 mo.	Hypoplasia	5 × 10 mg. on 5 days	+	
13	G.	21	2 yr.	Hypoplasia neg. vaginal smear	5 × 10 mg. on 5 days	-	
14	D.	23	3 yr.	Normal	5 × 10 mg. on 5 days	+	None
15	F.	18	3 yr.	Hypoplasia	5 × 10 mg. on 5 days	+	
16	F.	20	5 yr.	Hypoplasia	5 × 10 mg. on 5 days	+	
17	K.	26	7 yr.	Hypoplasia	5 × 10 mg. on 5 days	+	
18	G.	40	7 yr.	Highly atrophic	5 × 10 mg. on 5 days	-	
19	K.	26	7 yr.	Hypoplasia	Progestoral tablets 300 mg.	+	2 spontaneous periods of bleeding

estrogen production will probably account for the lack of response in the two other cases. In Case 13 the negative vaginal smear (using the method of Shorr and Papanicolaou) furnished a strong support for this assumption. There were masses of leucocytes and only a few epithelial cells in the smear, similar to that usually found in cases where ovarian function is absent. In Case 18 the uterus was highly atrophic and the patient suffered in addition from hyperthyroidism.

Fig. 2 is an example of a mucous membrane in the proliferative stage found on biopsy in the beginning of the bleeding in an amenorrheic woman following treatment with progesterone alone.

(c) *Permanent Results.*—The therapeutic results obtained up until now in connection with amenorrhea are very unsatisfactory. It is, indeed, possible to induce bleeding in a proliferative mucous membrane with estrogenic hormone, and there is, moreover, the possibility of inducing bleeding in a progestationally converted mucosa

by giving preliminary treatment with estrogenic hormone, followed by progesterone. Only in very few cases is the cycle re-established in this way. The question now arose as to whether or not the treatment with progesterone alone would be active along those lines. There are as yet only 9 cases at our disposal to report upon since the rest of our patients could not be followed up (Table II). Four of these 9 cases were negative, i.e., only one single period of bleeding occurred after progesterone treatment, and from then on the patient continued to be amenorrheic. In the other 5 cases, however, further cyclic bleeding was induced; in 2 cases the cycle recurred once, in two others twice and in one three times. The latter patient also reported pregnancy.

It was therefore possible to obtain improvement for several months in 50 per cent of the cases of amenorrhea by one series of treatments with progesterone, but even here no permanent success could be achieved.

(d) *Induction of Several Periods of Bleeding After Repeated Administration of Progesterone.*—Up to now it has been assumed that progesterone cannot become active unless it meets a perfectly proliferated mucous membrane, grown under the influence of estrogenic hormone. But the fact that it is possible to induce intracyclic hemorrhages clearly demonstrates that this does not hold true any longer. This means that progesterone is able to induce bleeding even in a mucous membrane which is but imperfectly developed. This is most instructively shown by the following: In secondary amenorrhea bleeding was achieved with 50 mg. of progesterone. After the bleeding had stopped, another course of progesterone was given, following an interval of a few days. This second course of treatment again produced bleeding of several days' duration. In two women we succeeded in producing three successive periods of bleeding by giving three courses of progesterone (Table III).

CASE 1.—F., aged 20 years, had been amenorrheic for five years. Administration of 50 mg. of progesterone, 10 mg. each on five successive days, produced bleeding of three days' duration, after an interval of sixty hours. As early as forty-eight hours after bleeding had stopped another five days' course of progesterone was given, and again bleeding of several days' duration took place.

CASE 2.—K. B., aged 19 years, had been amenorrheic for fourteen months. After five days' treatment with progesterone a period of bleeding of six days' duration occurred after an interval of sixty hours. This time we waited only one day after bleeding had ceased and then began the second course of treatment. After this, bleeding began again, viz., after an interval of seventy hours, and persisted for five days.

TABLE III. SEVERAL PERIODS OF BLEEDING OCCURRING AFTER SEVERAL COURSES OF PROGESTERONE TREATMENT IN SECONDARY AMENORRHEA

NO.	NAME	AGE	DURATION OF AMENORRHEA	UTERINE FINDINGS	PROGESTERONE (MG.)	HOW MANY COURSES OF TREATMENT	HOW MANY PERIODS OF BLEEDING
1	F.	20	5 yr.	Hypoplasia	50 mg. on 5 days	2	2
2	K.B.	19	14 mo.	Hypoplasia	50 mg. on 5 days	2	2
3	L.	40	6 mo.	Normal	50 mg. on 5 days	2	2
4	H.	32	6 mo.		50 mg. on 5 days	2	2
5	K.	26	7 yr.	Hypoplasia	50 mg. on 5 days	3	3
6	K.	19	1 yr.	Hypoplasia	50 mg. on 5 days	3	3

CASE 3.—L., aged 40 years, had been amenorrheic for six months. The development of this case was much the same as that of Case 2. Bleeding occurred after progesterone treatment, then a three days' interval followed, after which a second course of progesterone was given, and again bleeding was obtained.

CASE 4.—H., aged 32 years, had been amenorrheic for six months. After five days' administration of progesterone, bleeding began. After an interval of six days, another course of progesterone was given and another very copious bleeding occurred.

CASE 5.—K., aged 26 years, had been amenorrheic for seven years. The uterus was 4.5 cm. long and narrow. She was given progesterone over a period of five days (50 mg.). Bleeding took place from the ninth to the twelfth day. After another course of progesterone had been given from the fourteenth to the eighteenth day, bleeding occurred again on the twenty-second day and persisted up to the twenty-fifth day. After an interval of one day, a third course of treatment was given from the twenty-seventh to the thirty-first day, whereupon very copious bleeding occurred a third time on the thirty-fifth day and persisted up to the thirty-eighth day (Fig. 1).

CASE 6.—K., aged 19 years, had been amenorrheic for a year. After five days' treatment with 50 mg. of progesterone, bleeding set in on the eighth day and lasted until the eleventh day. The second course was given from the thirteenth to the seventeenth day and bleeding took place a second time from the twentieth to the twenty-third day. After having waited one day, the third course of progesterone was given from the twenty-fifth to the twenty-ninth day, and on the thirty-second day bleeding occurred a third time and persisted up to the thirty-fifth day.

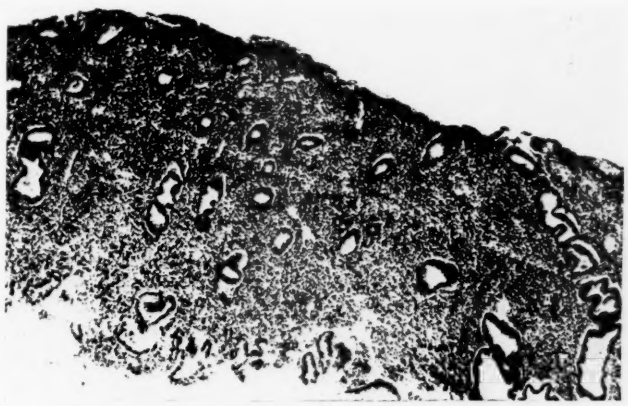


Fig. 1.—Photomicrograph of the uterine mucosa taken from a biopsy at the onset of intracyclic bleeding in a woman with a normal cycle. The patient had 50 mg. of progesterone in all, administered intramuscularly from the eighth to twelfth day of the cycle. Bleeding occurred on the fourteenth day of the cycle and lasted for three days, from a proliferative endometrium.

From the above we may conclude that, in secondary amenorrhea, it is possible to induce successive periods of bleeding, although there are only very short intermediate periods during which the mucous membrane can be only very slightly developed. No information is, however, as yet available as to how far it may be possible to start the menstrual cycle again by repeated courses of progesterone treatment. This will be reported upon later, when the patients will have been under observation for a greater length of time.

III. BLEEDING IN PRIMARY AMENORRHEA THROUGH PROGESTERONE AND SMALL QUANTITIES OF ESTROGENS

At the beginning of this paper it has been pointed out that, while it is possible to induce bleeding in secondary amenorrhea by treating the

patient with progesterone alone, this is not the case with primary amenorrhea. This led us to conclude that a certain degree of estrogenic hormone production must necessarily be present in the organism should bleeding actually occur. The fact, however, that it was possible, as in our cases of secondary amenorrhea, to induce several periods of bleeding following each other at short intervals suggests that the stimulus exerted by estrogens on the uterine mucosa need only be of the slightest degree. In view of this observation, we tried to stimulate the uterine mucous membrane through a very short preliminary treatment with estradiol benzoate, and then followed with progesterone. Over a period of no more than four days we gave a total of 20,000 I.B.U. of estradiol benzoate whereupon a five days' treatment with progesterone followed.* In those 3 patients who up to the present have been treated in this way, bleeding

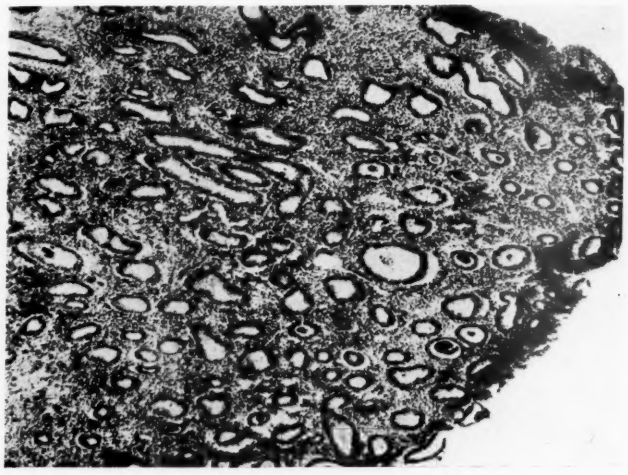


Fig. 2.—Photomicrograph of the uterine mucosa taken from a biopsy at the onset of progesterone-induced bleeding in a patient with secondary amenorrhea (fifteen months). The patient received 50 mg. of progesterone in all, administered intramuscularly during five days. At the seventh day bleeding occurred and lasted for three days, from a proliferative endometrium.

was actually obtained. In two further cases we chose another method, giving 20,000 I.B.U. of estradiol benzoate and 50 mg. of progesterone simultaneously, over a period of five days, and here, too, bleeding occurred.

CASE 1.—H., aged 34 years, had never menstruated. When she had undergone laparotomy, the ovaries were also inspected. They were of the size of a cherry, firm, and contained neither follicles nor corpora lutea, strongly resembling, therefore, those usually found in old women. A five days' course of progesterone (50 mg.) which had been given a year before had no effect. Now the patient was given 5,000 I.B.U. of estradiol benzoate daily over a period of four days, totaling 20,000 I.B.U. Then, from the fifth to the ninth day, a total of 50 mg. of progesterone was injected, and from the twelfth to the fifteenth day copious bleeding took place (Fig. 2).

*We are greatly indebted to Roche-Organon Inc., Nutley, N. J., for kindly supplying progesterone (progestin "Roche-Organon") as well as estradiol benzoate (dimenformon benzoate).

Biopsy on the onset of the bleeding revealed an extremely thin mucosa which contained only few glands in the postmenstrual stage.

CASE 2.—K., aged 30 years, had her ovaries removed. There were serious vasomotor deficiency symptoms. Five days' treatment with progesterone which had been given nine months before, had yielded no result. Now the patient received a total of 20,000 I.B.U. estradiol benzoate over a period of four days and, subsequently, a total of 50 mg. progesterone from the fifth to the ninth day, whereupon, on the twelfth day, bleeding appeared and persisted for three days.

CASE 3.—F., aged 39 years, had never menstruated. She was given 20,000 I.B.U. of estradiol benzoate in all over a period of four days, and, subsequent to this, 50 mg. of progesterone from the fifth to the ninth day. Copious bleeding set in on the twelfth day and persisted up to the fifteenth day.

CASE 4.—K., aged 30 years, had her ovaries removed. This patient was given 4,000 I.B.U. of estradiol benzoate and 10 mg. of progesterone simultaneously daily on five successive days (thus receiving a total of 20,000 I.B.U. of estrone and 50 mg. of progesterone). After the lapse of sixty hours (on the eighth day), bleeding of two days' duration took place.

CASE 5.—H., aged 34 years, had never menstruated. She received 4,000 I.B.U. of estrone and 10 mg. of progesterone simultaneously daily over a period of five days, a total, therefore, of 20,000 I.B.U. of estrone and 50 mg. of progesterone. On the ninth day bleeding of one day's duration appeared.

DISCUSSION

Up to the present it has been assumed that the corpus luteum hormone (progesterone) is only able to produce bleeding of the uterine mucosa, provided that estrogenic hormone has previously been active in bringing about perfect proliferation of the mucous membrane. The present investigations, however, make it clear that it is possible to induce bleeding during the intermenstrual stage (intracyclic bleeding) which takes place from an imperfectly proliferated mucous membrane (as has been verified by biopsy). It is, therefore, no prerequisite for the occurrence of a progesterone-produced bleeding that perfect proliferation be present. These observations were applied in the treatment of amenorrheic women (secondary amenorrhea), and it became evident that to induce bleeding did not require preliminary treatment with estrogens. Seventeen out of 19 cases were successfully treated in this way. It is worthy of record that several periods of bleeding in succession could be induced (e.g., three times during the course of one month) if another course of progesterone was started one to two days after bleeding had stopped. It is, therefore, irrelevant whether the mucous membrane from which bleeding occurs shows only slight or marked proliferation or has even been progestationally converted. The presence of a certain degree of estrogenic hormone production is, as a matter of fact, a prerequisite condition for the appearance of bleeding. Probably, the mucous membrane must be stimulated to a certain extent by this estrone produced in the organism. This is clearly shown by the fact that in primary amenorrhea no result is obtained by treatment with progesterone alone. It is, however, also possible to induce bleeding in primary amenorrhea, provided that small amounts of estrogens are also given, previously to or simultaneously with progesterone.

During pregnancy[3] even large doses of progesterone (up to 150 mg.) are unable to produce bleeding, and it is, therefore, impossible to induce abortion in this way.

In order that the intracyclic bleeding may take place, a certain interval between exogenous hormone administration and endogenous hormone production is required. If progesterone administration is started at the time of follicular rupture, which means at a stage when progesterone production in the patient's own organism has already begun, no intracyclic bleeding occurs.

Large doses of estrogenic hormone (100,000 I.U. estradiol benzoate, given daily over a period of four days) are active in preventing the intracyclic bleeding and are also able to delay normal menstruation, which must be attributed to impaired gonadotropic secretion in the anterior pituitary lobe (Zondek[4] 1935/36). Estrogenic hormone must, therefore, be held responsible for three functions: (a) Proliferation of the uterine mucosa, if the amounts administered do not exceed physiologic limits; (b) counteracting the activity of progesterone, if the amounts administered are higher than those physiologically present in the organism; (c) influence on the gonadotropic secretion of the anterior pituitary lobe.

SUMMARY

1. Bleeding of three to five days' duration is induced during the intermenstrual stage by a total of 50 mg. of progesterone given in the postmenstrual stage (intracyclic bleeding).

2. If progesterone is given at the time of follicular rupture, no intracyclic bleeding will occur. There must necessarily be an interval between exogenous progesterone administration and endogenous hormone production. Continuous administration of progesterone over the whole of the cycle produces no intracyclic bleeding either.

3. Pregneninonol per os has the same effect as progesterone given parenterally.

4. It is possible to prevent the occurrence of the intracyclic progesterone-produced bleeding through large doses of estrogenic hormone.

5. In secondary amenorrhea, it is possible to cause bleeding of three to five days' duration by giving a total of 50 mg. of progesterone split up in five doses and given on five successive days; bleeding then appears after an interval of sixty to seventy-two hours.

This bleeding takes place from a proliferatively developed mucous membrane. Seventeen out of 19 cases responded favorably. Instead of five days, 50 mg. of progesterone may also be distributed over two days only; however, if given in one injection, no result is obtained.

6. In roughly 50 per cent of our cases, one course of progesterone was able to improve secondary amenorrhea for several months. Permanent success has not been recorded as yet.

7. After bleeding which has been induced in secondary amenorrhea by progesterone treatment has stopped, another course of progesterone may follow immediately, which, in turn, will also produce bleeding. All

6 patients treated in this way showed a satisfactory response. In two of them bleeding was produced three times during the course of one month.

8. Progesterone is able to produce bleeding in an extremely thin mucous membrane which shows only slight evidence of proliferation as well as in the fully developed proliferative one and, likewise, in the progestational mucous membrane.

9. In primary amenorrhea treatment with progesterone alone fails. Bleeding can, however, be obtained if small amounts of estrogens are also given, either a few days previous to or simultaneously with progesterone.

10. No bleeding is obtained by progesterone treatment during pregnancy.

REFERENCES

(1) *Zondek, B., and Rozin, S.:* J. Obst. & Gynaec. Brit. Emp. **45**: 919, 1939; **46**: 736, 1939. (2) *Zondek, B., and Rozin, S.:* Lancet **1**: 504, 1939. (3) *Zondek, B.:* See reference 1. (4) Idem: Hormone d. Ovariums u. d. Hypophysenvorderlappens, ed. 2, Julius Springer, Vienna, 1935, pp. 387, 499, 507, and 508; Wien. klin. Wchnschr. **49**: 1282, 1936.

CALCIUM, PHOSPHORUS, AND NITROGEN METABOLISM IN WOMEN DURING THE SECOND HALF OF PREGNANCY AND IN EARLY LACTATION*

FRED W. OBERST,† PH.D., LEXINGTON, KY., AND E. D. PLASS, M.D., IOWA CITY, IA.

(From the Department of Obstetrics and Gynecology, State University of Iowa, Iowa City, Iowa)

THE metabolism of calcium, phosphorus, and nitrogen has been studied by a few investigators, but the complicated character of accurate balance experiments has interfered with the accumulation of many data on the various problems involved. This report covers metabolic studies of five pregnant women over some months of gestation, and of three of these patients during the first part of the lactation period. In order to present the data in the most comprehensive form, the results will be reviewed separately.

SUBJECTS

The subjects were 5 young primigravidas admitted to the Obstetric Service especially for this study, and maintained in separate quarters where they were constantly (day and night) under the supervision of a graduate nurse who had no other duties. A certain amount of work was required from each subject to provide sufficient exercise. They also were allowed to spend several hours daily on the hospital roof for fresh air and sunshine. Essential clinical data on each subject are shown in Table I.

*Received for publication, April 6, 1940.

†Now Biological Chemist at the U. S. Public Health Service Hospital.

TABLE I. DATA CONCERNING THE FIVE SUBJECTS

SUBJECTS, HOSPITAL CASE NO.	F-1088	F-1041	A-260	F-795	F-1540
Age	18	17	17	17	17
Height (inches)	?	66	66¼	62	59
Weight in kilograms at onset of experiment	58.1	53.6	74.9	59.5	45.4
Physical condition	Excellent	Excellent	Diabetes Gonorrhea	Syphilis treated	Excellent
No. of previous pregnancies	0	0	0	0	0
Onset last menstrual period	10-8-30	10-7-30	9-16-30	8-9-30	9-10-30
Date of first fetal movements	?	?	February (early)	12-27-30	2-7-31
Health during experiment	Good	Good. Had cold in Feb.	Good	Good	Good
Total gain in weight from first metabolism period until delivery (kilograms)	9.8	17.0	9.8	10.4	10.6
Duration of pregnancy (days)*	291	281	293	280	278
Date of parturition	6-4-31	7-15-31	7-6-31	5-16-31	6-15-31
Character of labor	Low forceps. Prolapsed cord	Spontaneous	Spontaneous	Low forceps. Inertia	Spontaneous
Weight of child (grams)	3600	3870	3428	3494	3008
Mother's convalescence	Slightly febrile second to eighth day	Afebrile	Afebrile	Febrile seventeenth to twenty-second day	Afebrile
Quantity of milk	Stillbirth	Insufficient	Insufficient	Satisfactory	Satisfactory

*Calculated from first day of last menstrual period.

DIET USED

The diets given during the entire period of study were based upon the general prenatal diet* recommended by the Department of Pediatrics, State University of Iowa. Four different arrangements of the recommended foods, Diets A, B, C, and D,† were planned to relieve monotony.

*A minimum of a quart of milk per day; a minimum of one egg; 1 moderate serving of meat or fish; 2 vegetables (one-half cup minimum serving); 2 fruits, 1 of which was served raw (one-half cup minimum serving); 1 teaspoonful cod liver oil; 6 teaspoonfuls butter (one ounce); other foods as bread, cereal, potatoes, were added to satisfy the appetite.

The vegetables were divided into two classes: (1) lettuce, spinach, tomatoes, celery, cauliflower, string beans, asparagus, chard, and cabbage; (2) peas, carrots, beets, turnips, parsnips, onions, rutabagas, eggplant, and squash. Both vegetables might be taken at a serving from class (1) but only one could be taken from class (2).

The fruits from which selections were made were: oranges, grapefruit, apples, peaches, apricots, plums, prunes, pears, and berries. These were either fresh, canned, or dried. Bananas were not served more than twice a week.

†Diets A and B are listed in detailed form as follows (all of the figures are the weight in grams):

Diet A: Breakfast: Cream 75; sugar 20; orange juice 170; butter 10; toast 20; cornflakes 20; egg 50; cocoa made with milk 200, sugar 10, cocoa 5, and several drops of vanilla.

10:00 A.M.: Milk 170; one orange; cod liver oil 6 Gm. followed by 5 Gm. grape juice.

(*Continued at bottom of next page.*)

Each of the four diets had practically the same calcium, phosphorus, and nitrogen content as well as the same caloric value. In determining the amount of food necessary for the subjects, individual variations in size and weight were considered. Diet A was given to the three subjects who weighed from 53 to 59 kilograms at the beginning of the experiment. In this diet the daily intake was approximately as follows: calcium 2.1, phosphorus 1.9, nitrogen 14, fat 168, and carbohydrate 252 Gm., with a total caloric value of approximately 2,954 calories. Another subject, F-1540, weighing 45 kilograms at the beginning of the experiment, received about 10 per cent less food. The diet for the diabetic subject, A-260, weighing 74 kilograms, was arranged to conform with those used in regular diabetic management. It was essentially the same as listed in Diets A, B, C, and D, except there was an increase in fats and a decrease in carbohydrates. Her daily intake, with the exception of the first period, was approximately as follows: calcium 2.5, phosphorus 1.9, nitrogen 15, fat 218, and carbohydrate 172 Gm., with a caloric value of approximately 3,139 calories. The diet given during the first period, having a caloric value of about 2,000 calories and a correspondingly lower calcium, phosphorus, and nitrogen content, proved inadequate to maintain her body weight.

EXPERIMENTAL

The metabolic balances were determined from a ten-day analysis period made once each month. The food was weighed in the diet kitchen and checked by the nurse in charge of the subjects. Diet A was given each day during the ten-day collection period, while Diets B, C, and D were given on successive days between the collection periods to prevent monotony. During the collection periods, an additional serving of Diet A, with the exception of milk and cream, was prepared with each meal and saved for chemical analysis to determine the total intake. This was preserved in a large covered beaker containing sufficient 15 per cent sulfuric acid for its chemical digestion. Since milk from a large dairy herd does not vary appreciably in chemical composition from day to day, only one sample of milk and cream was analyzed during each collection period. Water used by the subjects was carefully measured

---

Dinner: Milk 200; mashed potatoes 50, with butter 10; butter 10; tomatoes 100, with butter 10; grated beef cake 60, with butter 5; shredded lettuce 40, with mayonnaise 5; bread 20; ice cream 100.
3:00 P.M.: Malted milk consisting of milk 133, ice cream 33, and malt 10.
Supper: Cottage cheese 45, with cream 25; baked potatoes 75, with butter 5; bread 20; butter 10; peas 10, with butter 5; milk 170; canned peaches 120.
8:00 P.M.: Milk 250.

Diet B: Breakfast: Cocoa consisting of milk 200, sugar 10, cocoa 5 and a few drops of vanilla; cream 100; grapefruit sections 100; shredded wheat 20; toast 20; butter 10; egg 50; sugar 10.
10:00 A.M.: Milk 170; one orange.
Dinner: Milk 200; bread 20; butter 10; baked potatoes 50, with butter 10; liver 50, with butter 5; celery 20; sliced apples 50; ice cream 100.
3:00 P.M.: Malted milk consisting of milk 133, ice cream 33, and malt 10.
Supper: Milk 170; bread 20; butter 10; rice 20; sugar 10; string beans 100, with butter 10; deviled egg 50; canned pears 120.
8:00 P.M.: Milk 250.

Diets C and D: These were similar to Diets A and B, the difference being that some of the food products were substituted by a similar product from the recommended list of foods.

and its calcium content determined by analysis. The subjects were expected to eat all the food given them, but when any was refused, it was weighed and preserved in 15 per cent sulfuric acid for separate analysis.

During each metabolic period twenty-four-hour urine collections were made. The daily output was thoroughly mixed, measured, and a portion preserved with toluene for analysis. Feces for the entire period, marked by carmine administration at the beginning and end of each period, were collected and preserved in a covered beaker containing 15 per cent sulfuric acid. The breast milk from the subjects, after delivery, was obtained by means of an electric breast pump. One-tenth of each pumping was saved for analysis and the remainder given to the baby, supplemented, when necessary, by formulas. The separate milk specimens were pooled for the entire period and preserved in a refrigerator with a few drops of 30 per cent formalin.

Food, food refusals, and stools, preserved in 15 per cent sulfuric acid, were digested and analyzed according to the methods employed by Stearns.[1] Milk (including breast milk) and cream were analyzed separately, using the same technique. The total nitrogen of the urine was determined by the Kjeldahl method, while the Fiske and Subbarow method[2] was employed for the inorganic phosphorus. Urine calcium was determined by the method of McCrudden, as modified by Stearns, except that the calcium oxalate was separated by centrifuging rather than by filtering.

FETAL REQUIREMENTS FOR CALCIUM, PHOSPHORUS, AND NITROGEN

So far as the pregnant woman is concerned, the calcium, phosphorus, and nitrogen balances depend upon two factors: (a) the amount needed to supply the demands of the growing fetus and its adnexa, plus the maternal tissue increment and (b) the utilization of these substances ingested. Data on the former factor are available in several reports on mineral analysis of fetuses of different lengths at different periods of intrauterine development: Fehling,[3] Hugounenq,[4] DeLange,[5] Michel,[6] Schmitz,[7] Camerer,[8] Givens and Macy.[9] Coons[10, 11] has made an excellent review of this literature and has prepared tables and charts on mineral requirements for fetal growth.

The various data on fetal analyses for calcium, phosphorus, and nitrogen were combined and graphed against the period of gestation in weeks and the weight of the fetus according to Streeter's[12] tabulation. The average daily increment (in grams) accruing to the fetus in the eighth, ninth, and tenth lunar month is included in Table II.

RESULTS

Calcium.—Ante partum: It is apparent from the figures in Table II that the fetal requirement for calcium increases rapidly in the latter months of gestation, and that there must be a very considerable positive balance in the mother if her fixed stores of calcium are not to be depleted. A number of investigators have reported calcium balances in pregnant women, as summarized in Table II. In a number of these cases, the daily average retention of calcium was evidently not sufficient to meet the fetal requirements.

TABLE II. SUMMARY OF CALCIUM, PHOSPHORUS, AND NITROGEN BALANCE STUDIES. DAILY AVERAGE BALANCE (GRAMS)

INVESTIGATORS	NO. OF SUBJECTS	NO. OF PERIODS	CALCIUM		PHOSPHORUS		NITROGEN		REMARKS
			INTAKE	RETENTION	INTAKE	RETENTION	INTAKE	RETENTION	
Zacharjewsky[23]	6	6					11.55-24.08	0.95-5.37	Limited diet
Schrader[24]	2	2					22.20-22.54	5.97-6.75	Completed diet
Slemons[25]	4	4					13.80-16.77	0.42-4.72	Completed diet
Hahl[26]	2	7					15.89-20.79	0.60-4.11	
Bar and Daunay[21]	3	11*			2.75-4.30	−0.29-1.14	13.71-21.66	5.10-10.07	
Hoffström[13]	1	23	1.01-2.39	−0.33-0.95	1.15-2.86	−0.15-0.59	7.15-17.46	−1.21-3.53	Continuous observation
Landsberg[22]	6	8†			1.77-1.94	0.23-0.36	12.03-18.90	1.38-3.94	Periodic type of balance
Landsberg[14]	14	14	1.82-2.94	0.02-0.83	2.19-3.10	0.10-1.27	12.21-16.10	0.05-2.98	Self-chosen diet
Wilson[27]	3	37					7.88-19.72	0.46-6.37	Continuous observation
Coons-Blunt[15]	9	23	0.60-1.62	−0.11-0.29	0.94-2.21	−0.14-0.53	7.74-14.31	−0.43-8.45	Home diet
Sandiford et al.[28]	1	5					11.20-14.92	−1.90-1.10	Computed diet
Macy et al.[16]	3	12	1.53-2.69	−1.28-0.28	1.46-2.97	−0.16-0.53			Ordinary diet
Macy et al.[17]	1	2	1.55-1.93	0.62-0.64	1.76-1.99	0.17-0.39	11.50-12.20	2.20-2.90	Specified diet
Toverud[18]	16	27	0.58-1.69	−0.43-0.68	0.71-1.98	−0.61-0.74			Ordinary diet
Toverud[18]	23	30	0.81-2.16	0.26-0.90	0.71-2.63	−0.35-1.14			Regulated diet
Coons[10]	6	25	0.81-2.38	0.06-0.45	1.05-2.56	0.03-0.77	8.08-19.13	0.49-5.20	Home diet
Hunscher et al.[29]	3	12					11.58-23.58	−0.67-6.25	
This study	5	21	1.63-2.64	0.23-0.88	1.44-2.00	0.02-0.68	9.99-15.15	−0.77-3.65	Regulated diet
Daily amounts deposited in fetus during eighth, ninth, and tenth month, respectively, of intrauterine growth.			0.10, 0.25, 0.29		0.04, 0.16, 0.17		0.43, 0.62, 0.97		

*3 for nitrogen.

†13 for nitrogen.

TABLE III-A. TEN-DAY CALCIUM BALANCES IN PREGNANT WOMEN

(For daily values divide by 10)

	F-1088	F-1041	A-260	F-795	F-1540	AVE. PER DAY
Fifth Month						
Total intake		21.93				2.19
a. Solid food		5.73				0.58
b. Milk		15.55				1.56
c. Water		0.65				0.06
Total excretion		17.30				1.73
a. Urine		3.58				0.36
b. Feces		13.72				1.37
Retention		4.63				0.46
Sixth Month						
Total intake	21.99	21.13				2.15
a. Solid food	5.59	5.03				0.54
b. Milk	15.55	15.55				1.56
c. Water	0.85	0.55				0.07
Total excretion	17.56	16.08				1.68
a. Urine	5.24	3.73				0.45
b. Feces	12.32	12.35				1.23
Retention	4.33	5.05				0.47
Seventh Month						
Total intake	20.07	21.62	18.59	21.82	16.31	1.97
a. Solid food	4.58	5.34	5.62	5.55	2.98	0.48
b. Milk	14.68	15.55	11.70	15.30	12.84	1.40
c. Water	0.81	0.73	1.27	0.97	0.49	0.085
Total excretion	15.33	12.83	16.27	16.91	10.96	1.45
a. Urine	5.43	3.88	2.67	1.35	1.35	0.29
b. Feces	9.90	8.95	13.60	15.56	9.16	1.14
Retention	4.74	8.79	2.32	4.91	5.35	0.52
Eighth Month						
Total intake	21.81	21.05	25.63	20.46	19.23	2.16
a. Solid food	5.34	4.64	7.06	5.01	3.90	0.52
b. Milk	15.55	15.55	17.42	14.38	14.00	1.54
c. Water	0.92	0.86	1.15	1.07	1.33	0.11
Total excretion	14.15	15.13	18.89	16.69	14.63	1.59
a. Urine	5.26	4.18	2.89	1.54	1.73	0.31
b. Feces	8.89	10.95	16.00	15.15	12.90	1.28
Retention	7.66	5.92	6.74	3.77	4.60	0.57
Ninth Month						
Total intake	21.23	20.77	24.96	22.45	19.05	2.17
a. Solid food	4.64	4.44	6.80	5.34	3.32	0.49
b. Milk	15.55	15.55	17.42	15.55	14.00	1.56
c. Water	1.04	0.78	0.74	1.56	1.73	0.12
Total excretion	14.30	14.01	16.37	16.23	12.99	1.48
a. Urine	4.60	3.64	3.37	1.77	1.14	0.29
b. Feces	9.70	10.37	13.00	14.46	11.85	1.19
Retention	6.93	6.76	8.59	6.22	6.06	0.69
Tenth Month						
Total intake			26.39	21.84	19.97	2.27
a. Solid food			7.30	4.64	4.36	0.54
b. Milk			17.42	15.56	14.00	1.57
c. Water			1.67	1.64	1.61	0.16
Total excretion			18.62	17.12	14.35	1.67
a. Urine			2.12	1.66	0.35	0.14
b. Feces			16.50	15.46	14.00	1.53
Retention			7.77	4.72	5.62	0.60

The data on 21 ten-day metabolic study periods on calcium intake (solid food, milk, and water), output (feces and urine), and retention in 5 pregnant women from the fifth through the tenth month of gestation are presented. The daily intake for the subjects ranged from 1.63 to 2.64 Gm. and the retention from 0.23 to 0.88 Gm. In every case the calcium retention exceeded the required calcium deposition of the fetus. The lowest daily retention (0.23 Gm.) occurred in one individual during the seventh month when the fetal calcium requirement was still at a low level.

Post partum: Hunscher[20] has made calcium balance studies on 3 women in early lactation and found a negative calcium balance in spite of the high calcium intake. Macy and others,[19] in similar studies on 3 nursing mothers before and after supplementing their customary home diets with cod-liver oil and yeast, found that daily feedings of 15 Gm. of cod-liver oil and 10 Gm. of yeast over a period of two months, when the milk flow persisted at its maximum, stimulated better calcium and phosphorus utilization in all 3 patients.

The intake in 4 metabolic studies in early lactation varied from 1.92 to 2.18 Gm. and the retention from 0.024 to 0.511 Gm. per day. The retentions in subject F-795 were 0.07 Gm. per day in the first month after delivery and 0.02 in the second month. Her milk flow, however, was unusually good which undoubtedly

TABLE III-B. TEN-DAY CALCIUM BALANCES IN POST-PARTUM WOMEN

(For daily values divide by 10)

	A-260	F-795	F-1540
First Month	During the third week after delivery	During the first and second weeks after delivery	During the first and second weeks after delivery
Total intake	21.08	19.21	19.43
a. Solid food	4.58	3.23	4.61
b. Milk	16.50	14.59	13.61
c. Water	----	1.39	1.21
Total excretion	15.97	18.52	15.15
a. Urine	0.85	1.24	1.12
b. Feces	14.20	13.45	13.60
c. Breast milk	0.92	3.83	0.43
Retention	5.11	0.69	5.01
Second Month		During the fifth and sixth weeks after delivery	
Total intake		21.84	
a. Solid food		4.85	
b. Milk		15.55	
c. Water		1.44	
Total excretion		21.60	
a. Urine		2.70	
b. Feces		16.66	
c. Breast milk		2.24	
Retention		0.24	

accounted for these low values. The retentions of calcium in the other two subjects during the first month after delivery were much higher, being 0.51 and 0.50 Gm. per day, respectively. The quantity of milk secreted by them was, however, very much limited.

Phosphorus.—Ante partum: A summary of the literature on phosphorus balance studies in pregnant women is given in Table II. The daily phosphorus intakes and retentions among these subjects are quite variable. A number of them did not retain sufficient phosphorus for the fetal demand.

The detailed data concerning the phosphorus balances for our 5 subjects during 21 metabolic periods are presented in Table IV-A. The total daily intake ranged

TABLE IV-A. TEN-DAY PHOSPHORUS BALANCES IN PREGNANT WOMEN

(For daily average divide by 10)

	F-1088	F-1041	A-260	F-795	F-1540	AVE. PER DAY
Fifth Month:						
Total intake		20.25				2.03
a. Solid food		8.63				0.86
b. Milk		11.62				1.16
Total excretion		15.24				1.52
a. Urine		9.73				0.97
b. Feces		5.51				0.55
Retention		5.05				0.51
Sixth Month:						
Total intake	19.89	19.91				1.98
a. Solid food	8.27	8.29				0.85
b. Milk	11.62	11.62				1.16
Total excretion	14.79	13.12				1.40
a. Urine	10.64	7.44				0.90
b. Feces	4.15	5.68				0.49
Retention	4.90	6.79				0.58
Seventh Month:						
Total intake	18.45	19.32	14.57	19.66	14.41	1.73
a. Solid food	7.48	7.70	5.94	8.23	4.81	0.68
b. Milk	10.97	11.62	8.63	11.43	9.60	1.05
Total excretion	12.15	15.16	14.35	14.94	13.36	1.40
a. Urine	8.64	10.13	9.43	9.42	7.06	0.89
b. Feces	3.51	5.03	4.92	5.52	6.30	0.51
Retention	6.30	4.16	0.22	4.72	1.05	0.33
Eighth Month:						
Total intake	19.32	19.27	19.51	18.91	17.46	1.89
a. Solid food	7.70	7.65	6.66	8.16	7.02	0.75
b. Milk	11.62	11.62	12.85	10.75	10.44	1.15
Total excretion	12.97	16.25	16.27	15.24	14.08	1.50
a. Urine	9.57	12.01	11.42	9.39	9.18	1.03
b. Feces	3.40	4.24	4.85	5.85	4.90	0.46
Retention	6.35	3.02	3.24	3.67	3.38	0.39
Ninth Month:						
Total intake	19.27	18.91	19.85	19.32	17.65	1.90
a. Solid food	7.65	7.29	7.00	7.70	7.21	0.74
b. Milk	11.62	11.62	12.85	11.62	10.44	1.16
Total excretion	15.04	15.20	15.24	15.59	14 08	1.50
a. Urine	11.42	10.92	11.91	10.14	9.01	1.07
b. Feces	3.62	4.28	3.33	5.45	5.07	0.44
Retention	4 23	3.71	4.61	3.73	3.57	0.40
Tenth Month:						
Total intake			19.55	19.28	17.48	1.88
a. Solid food			6.70	7.66	7.04	0.71
b. Milk			12.85	11.62	10.44	1.16
Total excretion			15.26	16.78	13.21	1.51
a. Urine			11.05	11.04	8.02	1.00
b. Feces			4.21	5.74	5.19	0.50
Retention			4.29	2.50	4.27	0.37

from 1.44 to 2.0 Gm. and the retention from 0.022 to 0.68 Gm. The lowest figure (0.022 Gm. per day retention) occurred in subject A-260, who was the largest woman of the group and did not receive sufficient food during that period to maintain her body weight. The amount was increased considerably the following month, so that the phosphorus intake was increased from 1.46 to 1.95 Gm. per day, and the retention rose from 0.02 to 0.32 Gm. In all of the other metabolic periods, the amount of phosphorus retained exceeded the amount needed for fetal development.

Post partum: Hunscher[20] has recorded observations on the phosphorus balance of 3 women in successive lactation periods. These women who had a number of previous pregnancies with prolonged and abundant flow of milk were in negative phosphorus balance from the sixth to the twenty-seventh weeks of lactation, even though they were receiving diets containing as much as 3 to 4 Gm. of phosphorus per day. Macy and others[19] also reported phosphorus balances on three nursing mothers before and after supplementing their customary home diets with cod-liver oil and yeast, which stimulated phosphorus utilization.

In the present report 4 ten-day phosphorus balance studies as early as the first and second weeks after delivery are given.

TABLE IV-B. TEN-DAY PHOSPHORUS BALANCES IN POST-PARTUM WOMEN

(For daily average, divide by 10)

	A-260	F-795	F-1540
First Month	During the third week after delivery	During the first and second weeks after delivery	During the first and second weeks after delivery
Total intake	18.94	17.01	15.90
a. Solid food	7.24	6.07	5.75
b. Milk	11.70	10.94	10.15
Total excretion	17.82	18.85	16.15
a. Urine	12.00	11.82	10.17
b. Feces	5.26	5.22	5.36
c. Breast Milk	0.56	1.81	0.62
Retention	1.12	−1.84	−0.25
Second Month		During the fifth and sixth weeks after delivery	
Total intake		19.53	
a. Solid food		7.91	
b. Milk		11.62	
Total excretion		17.42	
a. Urine		10.89	
b. Feces		5.54	
c. Breast Milk		0.99	
Retention		2.11	

In the first month after delivery one patient, A-260, showed a retention of 0.11 Gm. on a daily intake of 1.89 Gm. Her milk flow was not very strong and the phosphorus in the excreted milk averaged only 0.056 Gm. per day for the ten-day period. The other two patients, who produced larger quantities of milk, were in negative balance.

A second study was made during the second month after delivery on one of the subjects (F-795) who in the first month had been in negative balance. The phosphorus intake was increased from 1.70 to 1.95 Gm. per day, while the milk flow had diminished so that the amount of phosphorus in the milk decreased from 0.18 to 0.10 Gm. per day. The phosphorus retention was 0.21 Gm. per day in contrast to the negative balance during the first and second weeks after delivery.

Nitrogen.—Ante partum: A number of investigators have studied nitrogen balances in the latter part of gestation as summarized in Table II. It is apparent that an average woman on an adequate diet, containing at least 7.7 Gm. of nitrogen per day, will store nitrogen. This amount, however, may vary considerably among different individuals. The fetus and its adnexa as well as the maternal tissue increment require large amounts of nitrogen to maintain a positive nitrogen balance.

In the present study of the 21 balances from the fifth through the tenth month of gestation, the daily nitrogen intake ranged from 9.99 to 15.15 Gm. and the retention from −0.77 to 3.65 Gm. Subject F-1540 was in negative nitrogen balance during one of the metabolic periods, even though she consumed most of the food

TABLE V-A. TEN-DAY NITROGEN BALANCES IN PREGNANT WOMEN

(For daily average divide by 10)

	F-1088	F-1041	A-260	F-795	F-1540	AVE. PER DAY
Fifth Month						
Total intake		146.32				14.63
a. Solid food		84.49				8.45
b. Milk		61.83				6.18
Total excretion		109.85				10.99
a. Urine		98.01				9.80
b. Feces		11.84				1.18
Retention		36.47				3.65
Sixth Month						
Total intake	143.38	148.48				14.59
a. Solid food	81.55	86.65				8.41
b. Milk	61.83	61.83				6.18
Total excretion	109.69	114.72				11.22
a. Urine	98.29	103.60				10.09
b. Feces	11.40	11.12				1.13
Retention	33.69	33.76				3.37
Seventh Month						
Total intake	138.38	143.13	116.15	140.87	99.90	12.77
a. Solid food	80.01	81.30	69.80	80.05	48.84	7.20
b. Milk	58.37	61.83	46.35	60.82	51.06	5.57
Total excretion	114.10	113.77	112.00	112.99	96.65	10.99
a. Urine	102.80	102.74	103.21	98.98	79.27	9.74
b. Feces	11.30	11.03	8.79	14.01	17.38	1.25
Retention	24.28	29.36	4.15	27.87	3.25	1.78
Eighth Month						
Total intake	143.13	142.29	151.50	143.68	131.17	14.22
a. Solid food	81.30	80.46	82.50	86.53	75.50	8.13
b. Milk	61.83	61.83	69.00	57.15	55.67	6.11
Total excretion	109.27	126.28	133.51	113.69	138.85	12.43
a. Urine	96.00	114.92	121.53	99.11	126.32	11.16
b. Feces	13.27	11.36	11.98	14.58	12.53	1.27
Retention	33.86	16.01	17.99	29.99	−7.68*	2.42
Ninth Month						
Total intake	142.29	137.08	151.40	143.13	129.87	14.07
a. Solid food	80.46	75.25	82.40	81.30	74.20	7.87
b. Milk	61.83	61.83	69.00	61.83	55.67	6.20
Total excretion	121.63	118.03	122.71	118.18	110.32	11.82
a. Urine	108.23	108.35	110.85	104.40	97.60	10.59
b. Feces	13.40	9.68	11.86	13.78	12.72	1.23
Retention	20.66	19.05	28.69	24.95	19.55	2.26
Tenth Month						
Total intake			144.30	142.32	129.74	13.88
a. Solid food			75.30	80.50	74.07	7.66
b. Milk			69.00	61.82	55.67	6.22
Total excretion			127.33	133.86	112.82	12.47
a. Urine			111.65	119.70	99.76	11.04
b. Feces			15.68	14.16	13.06	1.43
Retention			16.97	8.46	16.92	1.41

*Not included in average per day.

offered. The retentions for the various metabolic periods are inexplicably variable, but in all but two instances the nitrogen retention exceeded the amount required for fetal growth, and may be assumed to have been sufficient for the maternal growth incident to pregnancy.

Post partum: Slemons,[25] Hahl,[26] Harding and Montgomery,[30] and Macy and others,[19] found that nitrogen balances usually were negative in the puerperium in spite of generous nitrogen intakes.

The total daily intake in the present study on 4 ten-day metabolic balances ranged from 11.6 to 16.8 Gm. The two subjects studied during the first and second weeks of the puerperium were in negative balance, whereas those investigated in the third, and in the fifth and sixth weeks after delivery were decidedly in positive balance.

TABLE V-B. TEN-DAY NITROGEN BALANCES IN POST-PARTUM WOMEN

(For daily average divide by 10)

	A-260	F-795	F-1540
First Month	During the Third Week After Delivery	During the First and Second Weeks After Delivery	During the First and Second Weeks After Delivery
Total intake	167.50	119.16	116.20
a. Solid food	99.40	60.98	62.09
b. Milk	68.10	58.18	54.11
Total excretion	156.70	130.77	138.79
a. Urine	141.10	112.91	116.24
b. Feces	10.10	15.12	15.58
c. Breast milk	5.50	2.74	6.97
Retention	10.80	−11.61	−22.59
Second Month		During the Fifth and Sixth Weeks After Delivery	
Total intake		152.19	
a. Solid food		90.36	
b. Milk		61.83	
Total excretion		122.12	
a. Urine		92.80	
b. Feces		15.82	
c. Breast milk		13.50	
Retention		30.07	

DISCUSSION

Pregnancy.—It was the purpose of this study to determine the calcium, phosphorus, and nitrogen metabolism in pregnant women under dietary conditions which, at the present time, are believed to be nearly ideal for the growth and development of the fetus without depleting the maternal organism of these elements. Coons[10] has made an excellent study of this subject and has presented a thorough review of the factors involved in the retention of these dietary constituents. Because the products of conception cause notable readjustments in the physiologic processes of the maternal organism, the pregnant woman is subjected to unaccustomed nutritional requirements for fetal growth, for the preparation of her own body tissues for parturition, and for the future elaboration of milk.

The most important factors in the utilization of calcium and phosphorus by man have been reviewed by Macy, Hunscher, McCosh, and Nims.[19] They believe that, even though the mineral intake may be adequate, the acid-base equilibrium of the body and the acid-base properties of the food play an important role in calcium excretion, and will determine the extent of retention. Shohl[31] has pointed out that an alkaline diet is strongly indicated for the best calcium and phosphorus utilization during pregnancy and lactation. The diet used in the present study was decidedly on the alkaline side, the amounts of basic constituents being about three times the acid constituents. The results, therefore, appear to support the contentions of Shohl.

In addition to the acid-base properties of food elements, Macy and others found that sufficient amounts of vitamins C and D and of ultraviolet light or sunshine were necessary for adequate calcium and phosphorus retention during pregnancy and lactation. Moreover, the best retention of these substances was obtained when the calcium-phosphorus ratio of the food was between 1.0 and 1.5, as a relative excess of either element tended to depress the retention of both. In this study the calcium-phosphorus ratio of the food was within these limits. Each woman in the present series received 6 Gm. of cod-liver oil followed by 5 Gm. of grape juice daily in addition to the fruit in the diet, which supplied considerable amounts of vitamins C and D. They were also exposed to a variable amount of sunshine. One subject, F-1540, who was ill part of the time during the first two metabolism periods, had a low retention of calcium, phosphorus, and nitrogen, but after she was given daily ten-minute ultraviolet radiations for about a month, the retentions were improved to the level of the other subjects.

Little is known regarding the factors affecting dental conditions in pregnancy.

Hanke[32] has stated that "The prevalence of dental caries during puberty and pregnancy is well recognized. The underlying predisposing factors in dental caries appear to be metabolic, and I believe that improper diet is the commonest predisposing factor in all dental conditions." At best, our knowledge regarding the role of nutrition in tooth formation and preservation in the life cycle of an individual is not well understood. The majority of dental surgeons and obstetricians believe that the incidence of dental caries is higher in pregnant than in nonpregnant women, living under similar dietary conditions. Among the 9 women studied by Coons and Blunt[15] only 3 were storing as much calcium as was demanded by the fetus. Associated with these low calcium retentions, there was evidence of maternal tooth decay and of poor bone formation, as determined by x-ray examinations on the eighth day after birth.

Throughout the present metabolic studies, the condition of the teeth was carefully observed since each subject had caries on admission. Periodic examinations of the teeth were made by a dental surgeon, the results of which have previously been reported.[33] All cavities originally recorded were left untouched and open to all extraneous influences; no dental restorative work was done. In no case did new dental caries develop. In one case there was complete arrest of decay for the period of the study, and a consistent improvement in the teeth of all subjects was noted over the entire period of observation.

It is well recognized by various investigators that numerous factors are involved in the storage of nitrogen in pregnant women. In addition to the nitrogen requirements of the fetus, it is necessary to consider the amounts required by the placenta, amniotic fluid, and maternal tissue gain. Furthermore, such factors as the nutritive state of the woman before pregnancy, the accustomed level of protein intake, the quality of protein, and the caloric intake in the form of carbohydrates and fats influence the basal requirements for maternal nitrogen storage. A review of the studies reported in the literature indicates that it is impossible to state the protein requirements of the pregnant woman except

within very wide limits. Our women with a protein intake ranging from 11 to 15 Gm. of nitrogen per day met their own protein requirements satisfactorily.

In an average diet approximately two-thirds to three-fourths of the calcium, over half of the phosphorus, and nearly half of the nitrogen intake is from milk or milk products. The importance of using large quantities of milk and certain of its prepared products during pregnancy can not be overemphasized. Certainly no other single food substance will supply these dietary constituents as abundantly as milk.

Lactation.—In addition to the maintenance of her own tissue, a lactating woman requires minerals for secretion in the milk. The minerals may be supplied from her food or from her own mineral reserve. The occurrence of osteomalacia in cows, goats, rats, and women after repeated pregnancies associated with negative calcium and phosphorus balances indicates that calcium must be withdrawn from the maternal organism under such adverse conditions. The quantity of minerals excreted in the milk will depend largely on the volume of milk produced, since the mineral concentration of the milk tends to remain fairly constant. The mineral demands for the production of milk alone may be equal to that required for maternal maintenance. The lactation requirements of one woman may be two or three times greater than those of another woman who is producing smaller quantities of milk. Macy, Hunscher, McCosh, and Nims,[19] reported that daily feedings of cod-liver oil and yeast stimulated better calcium and phosphorus utilization. The fecal excretion of both calcium and phosphorus was decreased, indicating a marked alteration in metabolism and accounting for the greater assimilation of these elements.

In the present study the same diet prescribed during pregnancy was used during the lactation period. Cod-liver oil was included as usual, but not yeast. These experiments were not continued long enough during the puerperium really to test the adequacy of the diet for lactation. It is, however, believed that the prescribed general diet used during pregnancy would be quite satisfactory for milk production, since there was a definite retention of calcium in all of the post-partum experiments. Moreover, in two of the periods both the phosphorus and nitrogen balances were positive. It is known to be difficult to maintain a woman in positive calcium, phosphorus, and nitrogen balance during the first few weeks after delivery.

It is believed that the pregnant woman on an adequate diet stores nitrogen in excess of the amount needed for the fetus, its adnexa, and the normal growth of the maternal reproductive organs. It has been pointed out by Harding[34] that at least a part of this excess protein is deposited as a labile reserve against the demands of lactation. However, not all of the labile nitrogen is available for milk formation, since immediately following parturition there is a marked nitrogen loss associated with involution of the uterus.

It has been demonstrated that the pregnant woman on a satisfactory diet will store calcium and phosphorus in excess of the fetal needs. It is believed that a significant portion of the calcium and phosphorus

retention may be stored in the trabeculae of the bones[35, 36] as a labile reserve supply which can be utilized during lactation. Hence, the better the storage of calcium, phosphorus, and nitrogen during gestation, the greater the reserve for lactation.

SUMMARY

1. A series of 21 ten-day calcium, phosphorus, and nitrogen balance experiments were made on 5 women between the twenty-first and the fortieth weeks of pregnancy. Three of these women were also studied during early lactation.

2. The experiments were planned to obtain the maximum retention of calcium, phosphorus, and nitrogen during pregnancy. The results indicate that this end was accomplished.

3. The daily calcium intake for the various subjects during pregnancy ranged from 1.63 to 2.64 Gm. and the daily retention from 0.23 to 0.88 Gm.

4. The calcium intake in 4 metabolic balances during lactation varied from 1.92 to 2.18 Gm. with retentions varying from 0.02 to 0.51 Gm. per day. The subjects with the highest milk excretion had the lowest retention.

5. The daily phosphorus intakes during pregnancy ranged from 1.44 to 2.0 with retentions from 0.022 to 0.68 Gm.

6. The daily phosphorus intakes in four periods during early lactation on three women ranged from 1.59 to 1.95 and the retentions from –0.18 to 0.21 Gm. The negative balances shown by two women occurred shortly after parturition.

7. The daily nitrogen intakes in 5 pregnant women ranged from 9.99 to 15.15 with retentions from –0.77 to 3.65 Gm. The negative balance appeared in a subject who was ill during the collection period.

8. The total nitrogen intake during early lactation ranged from 11.6 to 16.8 Gm. per day. Two ten-day collection periods during the first and second weeks of the puerperium gave negative balances. Two other periods, one in the third and one in the fifth and sixth weeks of the puerperium, showed definitely positive balances.

REFERENCES

(1) *Sterns, Genevieve:* J. Lab. & Clin. Med. **14:** 954, 1929. (2) *Fiske, C. H., and Subbarow, Y.:* J. Biol. Chem. **66:** 375, 1925. (3) *Fehling, H.:* Arch. f. Gynäk. **11:** 523, 1877. (4) *Hugounenq, L.:* J. de physiol. et de path. gén. **2:** 509, 1900. (5) *DeLange, C.:* Ztschr. f. Biol. **40:** 526, 1900. (6) *Michel, C.:* Compt. rend. Soc. de Biol. **51:** 422, 1899. (7) *Schmitz, E.:* Arch. f. Gynäk. **121:** 1, 1923. (8) *Camerer, W.:* Ztschr. f. Biol. **43:** 1, 1902. (9) *Givens, M. H., and Macy, I. G.:* J. Biol. Chem. **102:** 7, 1933. (10) *Coons, C. M.:* Okla. Agri. Exper. Sta. Bull., No. 223, 1935. (11) *Coons, C. M.:* Thesis, Univ. of Chicago, p. 6, 1929. (12) *Streeter, G. L.:* Contrib. Embryol. (Carnegie Inst.), Wash. **11:** 143, 1920. (13) *Hoffström, K. A.:* Skandinav. Arch. f. Physiol. **23:** 327, 1910. (14) *Landsberg, E.:* Ztschr. f. Geburtsh. u. Gynäk. **76:** 53, 1914. (15) *Coons, C. M., and Blunt, K.:* J. Biol. Chem. **86:** 1, 1930. (16) *Macy, I. G., Hunscher, H. A., Nims, B., and McCosh, S. S.:* J. Biol. Chem. **86:** 17, 1930. (17) *Macy, I. G., Donelson, E., Long, M. L., and Graham, A.:* J. Am. Dietet. A. **6:** 314, 1931. (18) *Toverud, K. U., and Toverud, G.:* Norsk. mag. f. laegevidensk. **90:** 1245, 1929; **91:** 53 and

286, 1930; **92**: 677, 1931; Acta paediat. **12**: Supplementum 2, 28, 1931. (19) *Macy, I. G., Hunscher, H. A., McCosh, S. S., and Nims, B.:* J. Biol. Chem. **86**: 59, 1930. (20) *Hunscher, H. A.:* J. Biol. Chem. **86**: 37, 1930. (21) *Bar, P., and Daunay, R.:* J. de physiol. et de path. gén. **7**: 832, 1905. (22) *Landsberg, E.:* Ztschr. Geburtsh. u. Gynäk. **71**: 163, 1912. (23) *Zacharjewsky, A. U.:* Ztschr. f. Biol. **30**: 368, 1894. (24) *Schrader, T.:* Arch. f. Gynäk. **60**: 534, 1900. (25) *Slemons, J. M.:* Johns Hopkins Hosp. Reports **12**: 111, 1904. (26) *Hahl, C.:* Arch. f. Gynäk. **75**: 31, 1905. (27) *Wilson, K. M.:* Bull. Johns Hopkins Hosp. **27**: 121, 1916. (28) *Sandiford, I., Wheeler, T., and Boothby, W. M.:* Am. J. Physiol. **96**: 191, 1931. (29) *Hunscher, H. A., Donelson, E., Nims, B., Kenyon, F., and Macy, I. G.:* J. Biol. Chem. **99**: 507, 1933. (30) *Harding, V. J., and Montgomery, R. C.:* Ibid. **73**: 27, 1927. (31) *Shohl, A. T.:* Physiol. Rev. **3**: 509, 1923. (32) *Hanke, M. T.:* J. Am. Dent. A. **16**: 2263, 1929. (33) *Drain, C. L., Plass, E. D., and Oberst, F. W.:* Abst. in J. Dent. Research **13**: 233, 1933. (34) *Harding, V. J.:* Physiol. Rev. **5**: 279, 1925. (35) *Bauer, W., Aub, J. C., and Albright, F.:* J. Exper. Med. **49**: 145, 1929. (36) *Idem:* J. Clin. Investigation **7**: 75, 1929.

EFFECT OF VITAMIN K ADMINISTERED TO PATIENTS IN LABOR*

J. E. FITZGERALD, M.D., AND AUGUSTA WEBSTER, M.D., CHICAGO, ILL.

SINCE its discovery by Dam,[1-5] vitamin K has been used successfully in the treatment of hemorrhagic disease of the newborn,[22-24] and in the management of obstructive jaundice, before and after operation.[14-18, 21]

A number of investigations have been made on the prothrombin content of human blood, especially that of the newborn.[31-35] The results of these determinations have been somewhat confusing because of the various methods used to determine the prothrombin level.[24] In the two-stage method,[27, 29, 30] prothrombin is changed to thrombin in a preliminary step, and the thrombin formed is then titrated by means of a dilution technique. This method is excellent for research purposes but is too complicated for routine clinical use. In the Quick[22, 28] method thromboplastin is added to blood plasma, and the supposition is that thrombin is rapidly built up to the clotting level, and clotting therefore occurs before all of the prothrombin has been converted. The rate at which prothrombin can be built up to the clotting level depends both on the amount of prothrombin present and upon its "controvertibility." This method, therefore, measures both the amount of prothrombin, and the convertibility of the prothrombin, and is a summation of these two factors. It does not show simply the *amount* of prothrombin present. It is the opinion of Owen, Hoffman, Ziffren and Smith[24] that conversion occurs quite rapidly in the plasma of newborn infants, and that this fact compensates for a relative deficiency in amount.

The "bedside" test of Smith and others[26] is similar in principle to the Quick method, except that the thromboplastin is added directly to whole blood instead of to plasma; it does not require centrifuging of the blood, and can be done as its name suggests at the bedside. Like the Quick test the amount of prothrombin present and the ease of its con-

*Presented at a meeting of the Chicago Gynecological Society, April 19, 1940.

vertibility into thrombin are both measured. This test gives a good clinical index of the tendency of the patient to bleed.

In the work which we are reporting we used a slight modification of the simplified bedside technique of Smith, Ziffren, Owen and Hoffman.

Briefly, the technique which we employed is as follows:

Fresh rabbit's brain is extracted with acetone until a fine powder is obtained as described by Quick.[28] It is then dried in the incubator, sealed in glass tubes, and stored in the icebox until needed. To make the thromboplastin, one-tenth of a gram of the dried brain is added to about 10 c.c. of normal saline and incubated for forty-five minutes. The mixture is then centrifuged at low speed, and the supernatant fluid is poured off. One-tenth cubic centimeter of thromboplastin thus obtained is placed in a small serologic tube, and enough fresh blood is added to make 1 c.c. The tube is then at once inverted over the finger to obtain complete mixing, and then tilted back and forth until clotting occurs. The time is carefully measured with a stop watch. The normal is determined each day. The calculation is then made by the equation,

$$\frac{\text{Clotting activity}}{\text{(in \% of normal)}} \text{ equals } \frac{\text{Clotting time of normal}}{\text{Clotting time of patient's blood}} \times 100\%.$$

If the patient's blood clots in fifty seconds and normal is twenty-five seconds, the clotting activity will be 50 per cent. Expressed in the equation it will be,

$$\text{Clotting activity equals } \frac{25}{50} \times 100 \text{ per cent equals } 50 \text{ per cent.}$$

A two-stage titration technique was used in the early experiments of Brinkhous, Smith and Warner,[29, 30] in which they reported plasma prothrombin level in young infants as less than half as high as in normal adults. In this early work they obtained 14 to 39 per cent of normal.

Quick and Grossman,[31] using the Quick method, reported a series of cases in the proceedings of the Society of Experimental Biology and Medicine, 1939, in which blood was obtained by venipuncture from healthy infants 3 to 7 days old, and their results showed that the prothrombin concentrations were essentially the same as for normal adults. Also, in an article published in January of this year, Quick and Grossman,[32] using the Quick method, report the concentration of prothrombin in cord blood of normal infants as 60 to 70 per cent of normal adult blood. Shortly after birth they showed there is a drop in the prothrombin level, and it may reach very low levels, but tends to return spontaneously to normal between the fifth and seventh day.

Waddell and Guerry[23] reported a series of 20 infants, in which they kept 10 as controls, and gave K orally to 10. They gave 1 c.c. on the first day of life and 0.5 c.c. on the second and third days. They used Quick's method of prothrombin determination and showed that the highest clotting times occurred between forty-eight and seventy-two hours after birth, thus showing a low prothrombin level at this time. There was considerably less individual variation in the clotting times of the infants receiving vitamin K, and the clotting time in this group tended to maintain a common level. Dam, Tage-Hansen and Plum[33] report a similar series in the December, 1939, *Lancet*, arriving at the same conclusions.

Hellman, Delfs, and Shettles[34, 35] from Johns Hopkins have reported low prothrombin levels in 31 full-term normal infants and 17 premature infants. The prematures in their series were considerably lower than the full terms. They gave 4,500 Almquist units of vitamin K each day to five mothers from fourteen to thirty-five days before delivery, and raised the prothrombin level markedly in both the mother and infant. They also succeeded in raising the mothers' and babies' levels by giving single doses of the vitamin during labor. These workers used cord blood for their determinations. Our results differ from theirs in that they obtained much lower levels in the untreated infants' cord blood than we observed. These workers used the two-stage technique in their observations.

In the current March 2 issue of the *Journal of the American Medical Association*, Kato and Poncher[36] report a microprothrombin test which requires only a drop (from 10 to 15 c. mm.) of blood and which therefore should prove very useful in work with newborn infants. This test measures the clotting time according to this particular system rather than the actual amount of prothrombin present. They had a large series of 173 newborn infants, on which they made 1,595 tests. They found the prothrombin clotting time to be prolonged on the first day of life,

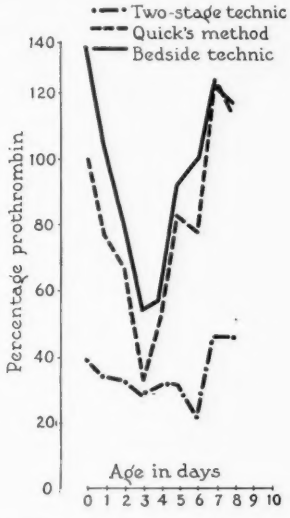


Fig. 1.—Average prothrombin levels in newborn by different techniques, from the figures of Owen, Hoffman, Ziffren and Smith.[24]

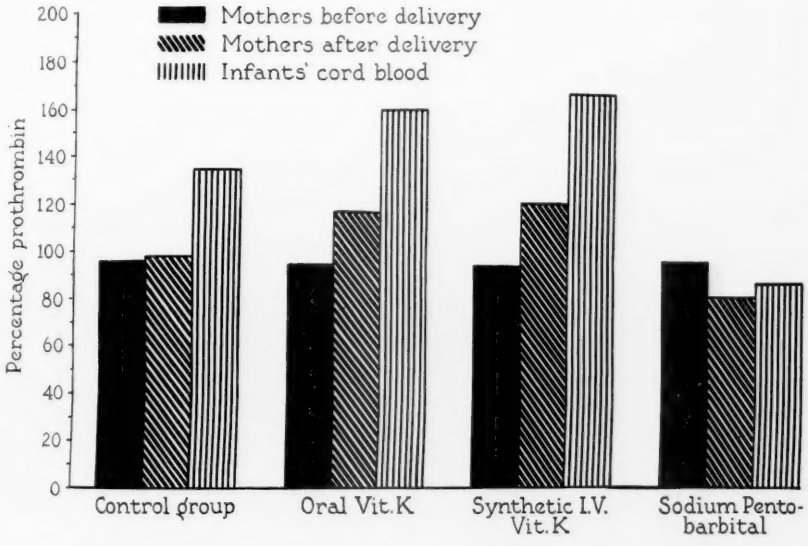


Fig. 2.—Graph showing average prothrombin readings in each group studied.

averaging 43.2 seconds for mature babies, and 46.5 seconds for immature babies, and that it gradually decreased so that the average on the tenth day was 25 seconds. The normal adult capillary whole blood clots in twenty seconds by this method. Their findings in the mature and immature infants were essentially the same.

In our study the Abbott preparation of Klotogen was used. This is put up in gelatin capsules, each of which contains 1,000 Almquist units. Each of these units is equivalent to approximately 37.5 Dam units. Four capsules were given in one dose during labor to each patient and 10 gr. of bile salts were given at the same time. Blood was drawn from the cubital vein of the mother before the K was given. At the time of delivery, blood was again taken from the mother and also from the umbilical cord of the infant. The percentage prothrombin was determined on each sample at the time it was obtained by the method described above. All of the tests were made by the same individual, who is a registered technician, and the same procedure was carried out in each case.

OBSERVATIONS

The patients used in this study were normal in all respects. They were at full term and free from venereal disease. They were all afebrile. In every case the blood pressure was within normal limits. There were no cases of prolonged labor and every patient delivered spontaneously, and no analgesic was used except where noted.

Table I shows the results in 25 untreated patients. Prothrombin levels were determined on the mother before and after delivery, and on the baby at birth. Determinations on the babies were made on cord blood. Investigation of the chart shows little difference in maternal prothrombin before and after delivery. Eight cases showed the prothrombin level slightly lower after labor; 14 showed slightly higher post-partum levels; 3 cases were the same before and after labor. The average maternal prothrombin before delivery was 95.2 per cent of normal; after labor it was 97.1 per cent. Such results suggest that normal labor has no effect on the maternal prothrombin, and that the method used for these determinations has a high degree of accuracy. The babies ranged in weight from 5 pounds 13 ounces

TABLE I. CONTROL GROUP

AGE	RACE	BLOOD PRESSURE	GRAV.	PROTHROMBIN		% CORD BLOOD	WT. OF BABY
				% ON ENTRANCE	% AT DELIVERY		
19	C	126/86	i	84	87	140	6 lb.
25	W	108/74	ii	85	85	125	6 lb. 7 oz.
21	C	120/84	i	87	83	118	6 lb. 5 oz.
21	W	110/60	i	88	83	120	6 lb. 5 oz.
19	W	119/76	i	92	86	130	8 lb. 9 oz.
16	C	120/70	i	92	92	96	6 lb. 1 oz.
22	W	110/65	i	93	90	190	6 lb. 6 oz.
25	C	90/70	v	93	95	139	8 lb. 7 oz.
22	C	136/96	i	95	92	122	7 lb. 5 oz.
29	C	120/90	i	95	96	144	6 lb. 4 oz.
30	W	132/60	ii	95	97	144	7 lb. 7 oz.
26	W	130/88	iii	95	97	119	6 lb. 5 oz.
22	C	98/50	iv	95	100	139	8 lb. 7 oz.
27	W	120/70	ii	95	103	130	7 lb. 5 oz.
24	C	112/74	i	97	96	105	7 lb. 2 oz.
31	C	118/65	i	97	99	134	7 lb. 9.5 oz.
15	C	120/80	i	98	100	144	5 lb. 13 oz.
18	W	120/68	i	98	107	139	6 lb. 8 oz.
23	C	132/80	iv	100	100	153	6 lb. 12 oz.
22	C	122/80	ii	100	105	123	7 lb. 12 oz.
23	C	132/80	iv	100	105	153	6 lb. 12 oz.
27	C	130/100	viii	100	107	139	8 lb. 7 oz.
17	C	126/80	i	104	108	162	6 lb. 8 oz.
23	W	110/65	iii	108	106	123	8 lb. 1 oz.
15	W	148/90	i	114	110	190	6 lb. 6 oz.
Average				96.1	97.1	135.2	

to 8 pounds 9 ounces. Prothrombin levels averaged 136.8 per cent of normal adult readings, and in every instance the prothrombin level in the babies' blood was higher than that of the maternal blood.

It should be remembered that throughout this discussion *prothrombin level* does not refer to the actual amount of prothrombin present in the blood, but rather to the *ability of the blood to clot,* which depends

TABLE II. GROUP RECEIVED ORALLY 4,000 ALMQUIST UNITS OF VITAMIN K AND 10 GR. OF BILE SALTS

AGE	RACE	BLOOD PRESSURE	GRAV.	BEFORE K %	TIME ELAPSED	AFTER K %	CORD %	WT. OF BABY
22	W	126/78	i	40	1 hr. 35 m.	59	104	6 lb. 9 oz.
18	C	124/82	i	57	1 hr.	66	109	8 lb. 1½ oz.
23	C	119/78	iii	69	1 hr. 55 m.	88	88	7 lb. 2 oz.
25	W	108/90	iii	70	6 hr.	97	143	7 lb. 10 oz.
27	C	127/82	i	73	3 hr. 55 m.	85	91	7 lb. 7 oz.
41	W	110/70	ix	78	3 hr.	114	192	6 lb. 14 oz.
15	C	102/88	i	81	2 hr. 25 m.	90	208	7 lb. 1 oz.
18	C	114/86	ii	82	9 hr.	92	115	6 lb. 11 oz.
22	W	128/74	i	83	9 hr. 40 m.	88	140	4 lb. 7 oz.
21	W	125/79	i	83	3½ hr.	192	158	5 lb. 14 oz.
36	W	135/86	v	85	3 hr.	96	114	6 lb. 10 oz.
25	W	108/80	ii	86	45 m.	109	141	6 lb. 10 oz.
19	W	104/54	i	88	2 hr. 40 m.	117	128	5 lb. 7 oz.
38	C	126/88	iv	90	3 hr. 35 m.	100	114	6 lb. 15 oz.
22	W	127/82	i	90	2 hr. 35 m.	148	220	8 lb. 2 oz.
19	C	114/78	ii	91	2 hr.	100	182	6 lb. 10 oz.
21	C	128/60	i	92	4 hr. 25 m.	115	170	7 lb. 2 oz.
21	C	134/74	i	93	26 hr.	114	240	8 lb. 12 oz.
23	W	110/80	ii	94	24 hr.	105	170	9 lb. 4 oz.
17	C	118/70	i	94	2 hr. 15 m.	124	167	6 lb. 9 oz.
22	W	140/98	i	94	5 hr.	120	247	6 lb. 6 oz.
22	W	132/88	i	95	4½ hr.	114	170	6 lb. 8 oz.
19	C	140/90	ii	95	4 hr. 20 m.	117	265	6 lb. 2 oz.
34	W	120/82	iv	95	5 hr.	119	145	9 lb.
19	W	120/70	i	95	9 hr.	130	130	4 lb. 6 oz.
21	C	136/80	i	95	1 hr. 45 m.	156	147	7 lb. 7½ oz.
22	W	120/80	iii	96	2 hr.	115	177	6 lb. 5 oz.
17	W	110/80	i	96	3 hr.	114	192	7 lb.
28	W	124/80	iii	96	4 hr.	120	141	7 lb.
32	W	120/80	i	100	3 hr.	105	105	6 lb. 10 oz.
24	C	128/82	ii	100	1 hr. 25 m.	107	160	7 lb. 2 oz.
18	W	134/90	i	100	1 hr. 30 m.	112	150	8 lb. 1 oz.
21	C	132/80	i	100	2½ hr.	120	148	6 lb. 7 oz.
25	W	138/80	iv	100	5 hr.	129	175	7 lb. 8 oz.
16	C	124/78	i	100	3 hr. 15 m.	170	170	7 lb. 5 oz.
17	W	104/60	i	103	4 hr. 20 m.	95	205	7 lb. 2 oz.
32	W	132/90	iv	104	5 hr.	109	135	7 lb. 8 oz.
24	C	98/68	iii	104	20 hr.	112	160	8 lb. 1 oz.
19	C	130/90	ii	104	4 hr.	121	153	8 lb. 2 oz.
25	C	130/78	iv	105	1 hr. 35 m.	112	136	7 lb. 6 oz.
16	C	136/88	i	105	3 hr.	124	181	5 lb. 13½ oz.
25	W	132/80	ii	105	3 hr. 35 m.	129	200	8 lb. 1 oz.
16	C	102/82	ii	106	3½ hr.	135	135	7 lb. 8 oz.
16	C	114/80	ii	108	10 hr. 55 m.	168	186	8 lb. 3 oz.
30	W	136/90	iv	109	1 hr. 10 m.	128	144	9 lb.
19	C	128/82	ii	110	6 hr. 35 m.	97	123	8 lb. 2 oz.
24	C	138/78	iii	111	1 hr. 15 m.	148	170	6 lb. 1 oz.
23	C	120/92	ii	113	2 hr.	131	160	8 lb. 14 oz.
22	C	120/70	ii	113	1 hr. 45 m.	133	200	7 lb. 5 oz.
20	C	138/96	ii	143	2½ hr.	190	266	7 lb. 5 oz.
Average				95.5		116.8	160.2	

upon the amount of prothrombin present and an X factor which governs the rate at which the prothrombin can be converted into thrombin. Thus it may be shown by a two-stage technique that the chemical level of prothrombin in the newborn is definitely lower than in a normal adult. Nevertheless our results show that routinely the cord blood of a full-term newborn infant clots faster than does that of the normal adult.

Table II shows the results of 50 cases in which the mother was given 4,000 Almquist units of vitamin K with 10 gr. of bile salts orally during labor. This medication was given from forty-five minutes to twenty-six hours before delivery. Forty-eight, or 96 per cent, of the mothers showed a higher prothrombin level at delivery than they showed before the administration of vitamin K. There is, of course, considerable variation in the prothrombin level of untreated cases, but regardless of the initial level the post-partum level was higher, except for the two cases noted. The average increase in prothrombin level was 21.3 points. The newborn showed a corresponding rise. The newborn of the untreated mothers all showed a higher level than that of the mothers. Of the newborn of the treated mothers, 94 per cent showed a prothrombin level higher than that of the mother at delivery, and 6 per cent showed the same level. This is significant because 96 per cent of the treated mothers showed a definite increase in prothrombin level, apparently due to treatment. The prothrombin level of the newborn of treated mothers was 160.2 per cent, compared to 135.2 per cent in the newborn of untreated mothers. Thus it seems clear that by the oral administration of Klotogen plus bile salts to a mother during labor there will result an elevation of the prothrombin level of both mother and child.

If the vitamin K be given intravenously in approximately the same doses (synthetic K – 2 methyl– 1:4 naphthoquinone), the results are similar. One dose of 2 mg. was given each of 19 patients (Table III). The time of administration was from fifty minutes to twenty-three hours and fifteen minutes before delivery. With one exception every mother showed a higher prothrombin level at delivery than before medication, and this one case was practically unchanged. Every cord blood showed a higher level than did the mother at delivery. The average gain for the mother was 26 points, and the babies averaged 30 points more than the babies of untreated mothers.

TABLE III. SYNTHETIC VITAMIN K

AGE	RACE	BLOOD PRESSURE	GRAV.	PROTHROMBIN		TIME ELAPSED	CORD %	WT. OF BABY
				% ON ENTRANCE	% ON DELIVERY			
19	C	136/86	i	71	92	3 hr. 50 m.	109	6 lb. 3 oz.
21	C	126/86	i	81	90	1 hr. 35 m.	135	7 lb. 4 oz.
22	W	------	iii	90	123	5 hr. 30 m.	142	7 lb. 3 oz.
24	C	130/88	iii	91	110	4 hr. 40 m.	216	7 lb. 1 oz.
16	C	104/60	i	92	103	2 hr. 20 m.	138	6 lb. 10 oz.
19	C	130/88	i	92	119	4 hr. 10 m.	165	7 lb. 10 oz.
17	C	116/70	i	93	110	1 hr. 55 m.	155	6 lb. 10 oz.
24	C	142/70	i	95	151	1 hr. 45 m.	180	7 lb.
32	W	122/80	i	96	115	2 hr. 20 m.	200	7 lb. 11 oz.
20	C	130/64	vi	97	110	1 hr. 35 m.	160	6 lb. 1 oz.
25	W	130/90	i	98	112	22 hr. 35 m.	118	9 lb. 3 oz.
28	W	118/70	iii	100	106	1 hr. 15 m.	165	7 lb. 8 oz.
23	W	------	i	100	113	2 hr. 45 m.	245	8 lb. 4 oz.
28	C	130/90	vii	100	122	50 m.	173	7 lb. 9 oz.
22	C	122/74	iii	100	133	55 m.	183	6 lb. 6 oz.
26	W	112/68	ii	100	165	23 hr. 15 m.	200	6 lb.
30	W	130/80	iv	100	169	2 hr. 35 m.	186	5 lb.
27	C	130/72	m	103	100	3 hr. 25 m.	189	7 lb. 15 oz.
28	C	138/86	iv	110	138	2 hr. 15 m.	138	7 lb. 4 oz.
Average				94.2	120.3		166.7	

TABLE IV. SODIUM PENTOBARBITAL GR. 7½

AGE	RACE	BLOOD PRESSURE	GRAV.	% PROTH. ON ENT.	TIME ELAP.	AT DEL. %	CORD %	WT. OF BABY
22	W	118/74	i	57	7 hr.	50	53	8 lb. 12 oz.
22	W	130/88	i	83	2 hr.	79	90	6 lb. 7 oz.
17	C	124/86	i	87	4 hr. 25 m.	68	100	8 lb.
22	W	130/90	i	92	9 hr. 35 m.	92	104	7 lb. 12 oz.
21	C	110/74	i	93	2 hr. 50 m.	84	140	6 lb. 7 oz.
22	C	130/80	i	96	5 hr. 25 m.	90	100	7 lb. 11 oz.
25	W	132/90	i	96	9 hr. 5 m.	90	104	6 lb. 9 oz.
19	C	138/88	i	97	8 hr.	90	60	7 lb. 2 oz.
18	C	120/80	i	98	3 hr. 30 m.	90	100	6 lb. 2 oz.
23	W	120/80	i	100	3 hr. 30 m.	74	92	6 lb. 2 oz.
18	C	114/62	i	100	3 hr. 50 m.	84	95	7 lb.
21	C	134/90	i	100	5 hr. 30 m.	89	121	7 lb. 10 oz.
27	C	138/84	ii	100	2 hr. 30 m.	90	104	6 lb. 9 oz.
23	W	122/94	i	100	1 hr. 10 m.	94	61	6 lb. 7 oz.
20	W	138/82	i	100	4 hr. 45 m.	103	60	6 lb.
19	C	128/62	ii	102	2 hr. 10 m.	90	60	6 lb. 2 oz.
20	W	130/88	i	103	2 hr.	106	63	7 lb. 3 oz.
28	W	110/80	i	104	9 hr.	80	73	8 lb.
31	W	120/78	iii	110	4 hr.	79	57	6 lb. 1 oz.
17	C	127/76	i	112	9 hr.	76	70	6 lb. 4 oz.
Average				96.5		80.4	85.3	

The cases considered so far have had no medication except the vitamin K. Table IV shows the results of a small series in which sodium pentobarbital was used as an analgesic. Of these 13 mothers only two had as high a prothrombin level at delivery as they did on entrance. The average loss was 14 points. This is in marked contrast to the untreated control group in which there was practically no variation in the prothrombin level before and after delivery. The findings in the newborn are still more striking. In less than half of the cases was the prothrombin level of the newborn as high as that of the mother at delivery and in 10 out of 13 the newborn prothrombin level was lower than that of the mother on entrance. The average prothrombin level of the newborn was 75.5 per cent, compared to an average level of 135.2 per cent in the untreated cases, and 160.2 per cent and 166.7 per cent of the treated cases. We are unable to explain this lower prothrombin level in the cases which had sodium pentobarbital as an analgesic. The method which we used for the determination of the prothrombin level measures the clotting ability of the blood, which depends upon the amount of prothrombin present and the rate at which it can be converted into thrombin. It seems reasonable to suppose that the actual amount of prothrombin in the mother and the newborn can hardly be diminished in so short a time, and that what happens is a disturbance of the rate at which the prothrombin can be converted.

TABLE V. NEMBUTAL GR. 7½ WITH VITAMIN K

AGE	RACE	BLOOD PRESSURE	GRAV.	BEFORE K AND NEMBUTAL %	TIME ELAP.	AFTER K %	CORD %	WT. OF BABY
21	W	128/82	i	96	32 hr.	51	78	7 lb. 4 oz.
22	W	148/84	i	76	8 hr.	74	44	7 lb. 1 oz.
20	C	98/56	i	143	2½ hr.	135	153	8 lb. 1 oz.
19	W	118/88	i	96	12 hr.	112	124	6 lb. 5½ oz.
20	W	128/84	i	104	3 hr. 30 m.	157	137	7 lb. 7 oz.
24	W	124/90	v	110	2 hr. 10 m.	105	105	9 lb.
18	C	146/70	i	84	1 hr. 35 m.	79	130	7 lb. 6 oz.
Average				709 101.3		713 101.8	771 110.1	

In an effort to determine whether or not we could prevent this change, we gave vitamin K (Table V) to a few patients who had the same drug for analgesia. The series is wholly inadequate for this purpose, because it is so small, but suggests the value of continued investigation along this line.

SUMMARY

1. A series of cases has been studied in an effort to determine the effect of vitamin K administered to women in labor.

2. Control cases show practically no change in the maternal prothrombin during and after labor.

3. Patients treated with oral klotogen during labor show a definite rise in the maternal prothrombin level at the end of labor. There is also a definite rise in the average level of the cord blood.

4. Patients treated with intravenous synthetic vitamin K show approximately the same elevation of prothrombin levels.

5. A small series of cases that was given sodium pentobarbital as an analgesic showed a definite depression in the prothrombin level of both mother and child.

6. This depression probably can be prevented by the proper use of vitamin K.

7. This paper should be considered as a preliminary report of work still in progress.

REFERENCES

(1) *Dam, H.:* Biochem. Ztschr. **215:** 475, 1929. (2) *Idem:* Ibid. **220:** 158, 1930. (3) *Dam, Henrik, and Schonheyder, Fritz:* Biochem. J. **28:** 1355, 1934. (4) *Dam, H.:* Biochem. J. **29:** 1273, 1935. (5) *Dam, H., Schonheyder, F., and Tage-Hansen, E.:* Biochem. J. **30:** 1075, 1936. (6) *Almquist, H. J., and Stockstad, E. L. R.:* Nature **136:** 31, 1935. (7) *Idem:* J. Nutrition **12:** 329, 1936. (8) *Clark, R. L. Jr., Dixon, C. F., Butt, H. R., and Snell, A. M.:* Proc. Staff Meet. Mayo Clinic **14:** 407, 1939. (9) *Smith, H. P., Warner, E. D., and Brinkhous, K. M.:* J. Exper. Med. **66:** 801, 1937. (10) *Greaves, J. D., and Schmidt, C. L. A.:* Proc. Soc. Exper. Biol. & Med. **37:** 43, 1937. (11) *Hawkins, W. B., and Brinkhous, K. M.:* J. Exper. Med. **63:** 795, 1936. (12) *Quick, A. J.:* Am. J. Physiol. **118:** 260, 1937. (13) *Quick, A. J., Stanley-Brown, Margaret, and Bancroft, F. W.:* Am. J. M. Sc. **190:** 501, 1935. (14) *Warner, E. D., Brinkhous, K. M., and Smith, H. P.:* Proc. Soc. Exper. Biol. & Med. **37:** 628, 1938. (15) *Butt, H. R., Snell, A. M., and Osterberg, A. E.:* Proc. Staff Meet., Mayo Clinic **13:** 74, 1938. (15) *Snell, A. M., Butt, H. R., and Osterberg, A. E.:* Am. J. Digest Dis. & Nutrition **5:** 590, 1938. (16) *Butt, H. R., Snell, A. M., and Osterberg, A. E.:* Proc. Staff Meet. Mayo Clinic. **13:** 753, 1938. (17) *Stewart, J. D., and Rourke, G. M.:* J. A. M. A. **113:** 2223, 1939. (18) *Smith, H. P., Ziffren, S. E., Owen, C. A., and Hoffman, G. R.:* J. A. M. A. **113:** 380, 1939. (19) *Ziffren, S. E., Owen, C. A., Hoffman, G. R., and Smith, H. P.:* Am. J. Clin. Path., Tech. Supp. **4:** 13, 1940. (20) *Scanlon, Geo. H., Brinkhous, K. M., Warner, E. D., Smith, H. P., and Flynn, J. E.:* J. A. M. A. **112:** 1898, 1939. (21) *Butt, H. R., Snell, A. M., and Osterberg, A. E.:* J. A. M. A. **113:** 383, 1939. (22) *Quick, A. J., and Grossman, A. M.:* Am. J. M. Sc. **199:** 1, 1940. (23) *Waddell, W. W., Jr., and Guerry, DuPont, III:* J. A. M. A. **112:** 2259, 1939. (24) *Owen, C. A., Hoffman, G. R., Ziffren, S. E., and Smith, H. P.:* Proc. Soc. Exper. Biol. & Med. **41:** 181, 1939. (25) *Quick, A. J.:* Am. J. Physiol. **114:** 282, 1936. (26) *Smith, H. P., Ziffren, S. E., Owen, C. A., and Hoffman, G. R.:* J. A. M. A. **113:** 380, 1939. (27) *Warner, E. D., Brinkhous, K. M., and Smith, H. P.:* Am. J. Physiol. **114:** 667, 1936. (28) *Quick, A. J.:* J. A. M. A. **110:** 1658, 1938. (29) *Brinkhous, K. M., Smith, H. P., and Warner, E. D.:* Am. J. M. Sc. **193:** 475, 1937. (30) *Warner, E. D., Brinkhous, K. M., and Smith, H. P.:* Am. J. Physiol. **114:** 667, 1936. (31) *Quick, A. J., and Grossman, A. M.:* Proc. Soc. Exper. Biol. & Med. **40:** 647, 1939. (32) *Idem:* Am. J. M. Sc. **199:** 1, 1940. (33) *Dam, H., Tage-Hansen, E., and Plum, P.:* Lancet **2:** 1157, 1939 (34) *Hellman, L. M., and Shettles,*

L. B.: Johns Hopkins Hosp. Bull. **65**: 138, 1939. (35) *Shettles, L. B., Delfs, E., and Hellman, L. M.:* Johns Hopkins Hosp. Bull. **65**: 419, 1939. (36) *Kato, K., and Poncher, H. G.:* J. A. M. A. **114**: 749, 1940.

104 S. MICHIGAN AVENUE
30 N. MICHIGAN AVENUE

DISCUSSION

DR. JOHN H. OLWIN.—As Dr. Fitzgerald has told you, there are at present three methods of measuring the prothrombin clotting activity of the blood, the Quick method, the bedside technique of the group at Iowa, where I feel the best work in this field is being done, and the two-stage method. As he mentioned, the one-stage method, either the Quick method or the bedside technique, measures not only the amount of prothrombin but the conversion activity of the prothrombin, and in addition the anticoagulant factors come into play. Fibrinogen and calcium vary little in the blood in most patients even in disease and this variation apparently has little effect on the clotting activity of the blood. The thromboplastic factor is highly variable and as yet we have no satisfactory method for measuring it, though Dr. Smith and his associates have laid the groundwork for such a test. In the two-stage method the plasma is first freed of fibrinogen, the prothrombin is converted to thrombin, and in a separate stage the thrombin is allowed to act on prepared beef fibrinogen. The number of units of prothrombin are estimated and compared to the number in normal control plasmas, thus giving the percentage of prothrombin in the plasma in question.

During the last seven or eight months in connection with our obstetric department, we have been studying prothrombin levels of normal pregnancy. These vary a great deal. Some of the women have as high as 150 per cent prothrombin levels during normal pregnancy. Some maintain these high levels practically throughout the course of pregnancy up to the time of delivery. Others drop to near normal or below. If they are running in the high brackets, they usually stay there. Some may vary as much as 50 points, however. Just why this great variation we do not know. Some we have studied began to taper off about term. Shortly after delivery, twenty-four to forty-eight hours, they begin to climb again. This may be on the basis of the concentration of the blood at this time. These determinations have been made by the two-stage method. Our studies are as yet very incomplete.

The two methods under discussion, the "bedside method" and the two-stage technique, roughly follow each other in the measure of prothrombin. Individual tests, however, may vary as much as 50 per cent. The percentage of error in the two-stage method is about 3 per cent. It should be borne in mind that one is measuring several factors, the other, so far as we can determine, only one factor.

During the last week we have studied 3 cases in which we have administered nembutal before delivery. These are certainly too few cases to draw conclusions on. (I have slides illustrating this study.) Two cases showed no appreciable change in prothrombin level following the administration of 6 gr. of nembutal. One case showed a drop of 18.5 per cent. Control cases receiving only ethylene showed a similar drop or no change at all. Our results, as you see, do not quite correspond to the results we have seen in the paper presented by Dr. Fitzgerald. In spite of that I feel the point of this paper is well taken.

There is good evidence to indicate that prothrombin is made in the liver. Hepatectomized dogs show an immediate marked drop in prothrombin. Dogs under chloroform anesthesia show a rapid fall in prothrombin and the return to normal level is commensurate with the time required for complete liver regeneration. Patients with toxic hepatitis, cirrhosis and acute yellow atrophy have a lowered blood prothrombin and respond poorly or not at all to vitamin K therapy.

Hrubetz and Blackberg in the last few years have studied several series of rabbits to which they administered nembutal, phenobarbital, and other barbiturates intraperitoneally, in order to study the effect of the drugs on the ability of the liver to mobilize glycogen. Normal rabbits show a marked increase in blood sugar after the injection of epinephrine. So far as we know the higher barbiturates, as nembutal, pentothal, etc., are detoxified in the liver. Phenobarbital on the other hand is eliminated by the kidneys. All of the barbiturates studied showed a

definite depressant effect on the glycogenolytic power of the liver. The mechanism of this effect is entirely speculative and will require further investigation. I feel there is definite promise in this type of study, not only from the point of view of the effect of barbiturates on the maternal body mechanism but also on that of the baby both before and after delivery. This is a study in itself and time will not permit a discussion of it at this time.

DR. W. J. DIECKMANN.—Attention must be called to the excellent work done by the biochemists. Vitamin K has only been known for several years and yet chemists have isolated and synthesized it.

Dr. Fitzgerald's data are interesting and his figures are all very exact. The prothrombin time and clotting time may vary. All reports to date indicate that vitamin K is of no value during the labor of normal patients to shorten the clotting time of the blood in the hope of preventing post-partum hemorrhage. Sufficient evidence has accumulated to show that the baby on the fifth or sixth day does have a decrease in its prothrombin time. If the baby shows any evidence of bleeding, vitamin K should be given. If the prothrombin time is prolonged and if facilities are not available for its determination, vitamin K should be given empirically. It is especially the premature baby that is likely to have a prolonged prothrombin time, and it may be found advisable to routinely administer vitamin K to these babies or to the mothers during labor. It may also be found advisable to administer vitamin K to the mother or to the baby where labor is long or the delivery difficult.

DR. FITZGERALD (closing).—I wonder if the cases in which Dr. Olwin found a variable prothrombin time before and after labor, had had some ethylene, and whether that might also be a factor.

As to Dr. Dieckmann's question, we made no investigation of the effect on babies of mothers who had either a long or a particularly difficult labor. This work is in progress now. We have presented a rather small series which may seem to show some very definite evidence that there may be an alteration in the prothrombin level of the mother and baby if treated during labor, and also that there is some good evidence that sedatives may lower this level. We were interested in finding out whether we could keep this level up by administering vitamin K. We are studying a series to find out what happens to the prothrombin level of the mother and baby in long labors, also in the premature baby and the effect of giving vitamin K to mothers in an effort to keep the fetal prothrombin level up to normal.

MORAL ASPECTS OF THERAPEUTIC ABORTION*

THOMAS V. MOORE, M.D., WASHINGTON, D. C.

WHEN the question is raised whether or not it is right to induce abortion, it implies that one may draw a conclusion one way or another in determining a stand on this important problem. Whenever a conclusion is drawn, there must be in the mind of the reasoner a general principle which determines what conclusion is to be deduced.

For many years physicians have considered themselves justified in performing an abortion when they considered that the physical well-being of the mother would be in serious jeopardy if a pregnancy were allowed to come to term. What principle governed the conclusion to which this general attitude may be ascribed?

The principle has thus been expressed by Hirst, in his textbook on obstetrics.

*Paper read at a symposium on Abortion at the Johns Hopkins Medical School, March 1, 1940.

The induction of abortion should be undertaken as reluctantly as one would commit justifiable homicide. If in the course of pregnancy some disease arises as a direct consequence of gestation, or if a woman suffering from disease is made much worse by the existence of pregnancy, and if her life is distinctly endangered in consequence, it is not only justifiable, but it is the physician's duty to terminate gestation, and thus to save one life, and that the more valuable of the two, instead of sacrificing both mother and fetus.[1]

We might crystallize the general principle embodied in this statement somewhat as follows:

Whenever the physician knows that the mother will die or her mental or physical health be seriously impaired if a pregnancy is allowed to go on to term and that he can save her life or her health by inducing an abortion, he has a right to kill the child in order that the mother may live and maintain her normal health.

There are three classes of cases to which the principle has been applied.

a. Those in which craniotomy has seemed to be the only possibility of saving the mother's life.

b. Cases of ectopic gestation.

c. Those in which pregnancy has been thought to be dangerous for the mother, should it be allowed to go on to term.

It is the latter problem with which this symposium is primarily concerned, but for the sake of rounding out the discussion I would first like to dwell briefly on the operation of craniotomy and the problem of ectopic gestation.

The operation of craniotomy involves two stages:

a. Perforation of the skull.

b. Complete destruction of the cerebral contents. In the words of De Lee, "the brain matter is thoroughly broken by means of a long forceps, taking special care to tear the tentorium and destroy the medulla, this to avoid the painful experience of seeing the child gasp after delivery."[2]

As I have pointed out in my *Principles of Ethics*,[3] the second stage of the operation became a general recommendation by reason of the fact that physicians from time to time were horrified by the delivery of a living child, in spite of the fact that much of its cerebral tissue had been destroyed.

From the fact now abundantly demonstrated that adults may survive very extensive removals of cerebral tissue and preserve mentality practically intact, one might well raise the question whether or not the child with its plastic nervous system might survive the loss of a considerable amount of cerebral tissue and still be able to develop a normal mental life.

If one looks into the literature, one will find cases of survival after craniotomy in spite of the fact that no steps were taken to control hemorrhage or limit the loss of cerebral tissue to the minimum required to reduce the cranial circumference so that delivery would be possible. The cases are few, but it would seem that a child may later manifest normal mentality in spite of delivery by craniotomy and may even live on into adult years.[4]

If this is the case, one may well ask what right has the physician to perform the second stage of craniotomy "to avoid the painful experience of seeing the child gasp after delivery"?

If the second stage of the operation is omitted and the physician attempts to effect delivery with as little loss of cerebral substance as possible and does all he can to save the life of the child, he is no longer making a direct attempt to kill the child but in certain rare instances in which delivery may be otherwise impossible, he will be doing all he possibly can do to save the lives, both of the child and of the mother.

Can he apply Hirst's principle to any such emergencies and say that he is attempting to save one life and that, the more valuable of the two, instead of sacrificing both mother and fetus, if he perforates the infant's skull and then makes a direct attempt to kill the child by a complete destruction of the cranial contents? The principle which seems so plausible simply does not apply, and the physician kills a child who might otherwise have lived and perhaps have become a normal human being.

The second problem is the termination of ectopic gestation. Until recently, the attitude of Catholic theologians has been that cases of ectopic gestation must be allowed to progress until an actual hemorrhage justifies intervention, lest the mother bleed to death. The principle has been maintained that the physician cannot lawfully kill the child by expulsion when it is not viable, even in order to save the mother's life. It has been the constant opinion of Catholic theologians that the extraction of a living nonviable child is a direct attack on its life and, therefore, contrary to sound morality.

Some years ago Vermeersch, a famous Jesuit, Professor of Moral Theology at the Gregorian University in Rome, had one of his students[5] study the problem in the light of pathology, and the following attitude was developed.

In normal pregnancy the placental villi grow into the thick uterine mucosa, breaking into capillary blood vessels, and so in the tiny surrounding spaces they are bathed with maternal blood and the fetus absorbs oxygen and nourishment from the mother. But when pregnancy occurs in the Fallopian tube, the thin mucosa is no longer an adequate barrier and the villi erode large blood vessels, so that the mother bleeds more or less severely into the tissues of the tube. A fatal termination is possible unless this bleeding is stopped. But it is always lawful to stop bleeding in order to save the patient's life, even if in so doing the death of a fetus would result. Thus one might imagine stab wounds producing hemorrhages which, if not controlled, would lead to the death of a pregnant woman, but of such a character that if the arteries are tied, the blood supply to the fetus is cut off and the fetus will die. Every Catholic theologian would recognize the right and the duty of the physician to control the hemorrhage in such a situation, even if in so doing the death of the fetus would be a concomitant result.

This is an example of the principle of double effect, perfectly logical and justifiable in itself, though at times difficult of application. It may thus be stated: Whenever two effects flow from one and the same act,

one good and the other bad, and the agent honestly intends the good effect, the act may be considered justifiable and the bad effect be looked upon as not aimed at or desired for its own sake.

When, therefore, a physician ties or clamps the Fallopian tubes on either side of an ectopic fetus and intends thereby to stop a hemorrhagic process which endangers the mother's life, his act is honestly an attempt to stop bleeding and not an attempt to kill a child.

Let us now turn to the problems of therapeutic abortion. If we look at Hirst's principle as applied to therapeutic abortion, it involves the three following statements.

I. If this pregnancy is not terminated promptly, the mother will die or her mental or physical health will be seriously impaired.

II. If this pregnancy is terminated promptly, the mother will live and her mental or physical health will be delivered from its present danger.

III. The physician has a right to kill the child in order to save the mother's life or in order to prevent serious impairment of her mental or physical health.

Let us postpone for a moment the discussion of the third proposition and turn to the first two propositions. When Hirst formulated the principle we have quoted, justifying therapeutic abortions, physicians in general were much more confident that they could say of a tuberculous mother, or one suffering from cardiac disease, or eclampsia, etc.: Unless this pregnancy is terminated promptly the mother will die.

Formerly therapeutic abortions were frequently undertaken in heart disease, tuberculosis, and eclampsia. But at the present day we may say that heart disease does not in itself indicate a termination of pregnancy before a viable child can be delivered. Thus, for example, Fitzgerald[6] reports the management of 126 women with heart disease during 192 pregnancies without the death of a single patient in pregnancy or labor.

The final conclusion of a very exhaustive study was that there is no evidence that tuberculosis is aggravated by pregnancy.[7]

Fovassier says in regard to abortions when the mother is tuberculous that the value of this procedure has not been certainly demonstrated at the Baudelocque Clinic and that "The sacrifice of the children is certain. The benefit to the mother is very often problematical."[8]

McNeile has pointed out that medical treatment of eclamptic patients has a much lower maternal mortality than the termination of pregnancy by therapeutic abortion.[9]

As to mental cases, Cheney says: "There appears to be no individual neurologic or psychiatric disorder that is an absolute indication for abortion in women suffering from such disorders"[10] and experience shows that patients with severe neurologic and mental diseases may go through pregnancy and have healthy children.

And so with the development of new methods of treatment and with the attempt made by various physicians to follow an expectant policy and treat the disease from which a pregnant woman might be suffering until a viable child might be delivered, it has become more and more evident that pregnancy may go on to term in spite of serious mental and physical disorders of the mother, and she may suffer no detriment or even improve by reason of the pregnancy, and a healthy child will be born at term.

It would seem, therefore, that one of the fundamental statements involved in the principle justifying therapeutic abortion cannot be made. No physician can say with certainty: If this pregnancy is not terminated promptly, the mother will die or her health be seriously impaired. On the other hand, he cannot say with certainty: If this pregnancy is terminated promptly by abortion, the mother will live.

Let us now look again at the principle by which therapeutic abortion is justified.

Whenever the physician knows that the mother will die if a pregnancy is allowed to go on to term and that he can save her life by inducing an abortion, he has a right to kill the child that the mother may live.

It would appear that one must introduce instead of "knows" some such phrase as "thinks it more likely" that the mother will die if pregnancy goes on to term, and that she may not die if she submits to an abortion.

What chance has the mother of living if she submits to an abortion? So much here depends on her own physical condition that statistics on mortality in general for abortions performed on healthy women by skilled physicians would give no pertinent information governing any individual case. Various German clinics report a mortality rate of 1.9 to 5.4 per cent.[11] The Russian operators who perform 25 to 30 abortions a day and are operating on healthy young women have a mortality rate of about one one-hundredth of 1 per cent.[12]

But when one performs a therapeutic abortion, he operates on a woman who is already seriously ill, and a great deal depends on her actual condition.

When, therefore, the problem of the physician's knowledge in relation to the outcome is looked at squarely, one must admit that:

a. The mother may die.

b. The fundamental disease, which was considered an indication for abortion, may be aggravated.[13]

c. Various remote results of an undesirable character may follow.

Thus Taussig reports on the Russian experiment: "Even the most enthusiastic of the Russian advocates of legalized abortion are, however, appalled at the growing evidence of serious pelvic disturbances, endocrine dysfunctions, sterility, ectopic pregnancy, and other complications following in the wake of artificial abortions."[14]

When confronted, therefore, with the problem of undertaking a therapeutic abortion, the physician of our day can no longer ease his conscience by taking refuge behind Hirst's principle: "It is not only justifiable, but it is the physician's duty to terminate gestation and thus to save one life and that the more valuable of the two, instead of sacrificing both the mother and the fetus."

He must envisage the following possibilities, and perhaps make to the family of the patient some such representations as these:

a. If the patient submits to an abortion, she may die from its effects, but in my own opinion she is more likely to live.

b. If she survives the abortion, the disease from which she is suffering may be aggravated, but I trust this will not be the case.

c. If she recovers, there may be various remote complications, such as pelvic disorders, dysmenorrhea, sterility, etc., and future pregnancies may be complicated and dangerous.

But, you may say, such statements are true in general. Suppose an individual case with all its attending circumstances in which the physician feels perfectly confident

a. that a therapeutic abortion will not endanger the mother's life.

b. that unless an abortion is performed and a nonviable child expelled from the uterus, the mother will certainly die.

May the physician under these circumstances perform a therapeutic abortion in order to save the mother's life?

One might answer such a question by merely saying that, as a matter of fact, no physician can ever be certain that the mother will not die from a therapeutic abortion or that she will certainly die unless it is performed. But the question raises the problem whether or not the physician is ever justified in taking a human life, directly and by explicit intention, and this problem is fundamental in the whole discussion.

Let us turn to the consideration of this problem.

Has any man a right to kill one man in order that another may live? Suppose an observer watching two men struggling for a life preserver. Both sink when both have hold of it, but it can support either alone. The man on shore has a rifle. Suppose he says: If I don't shoot one, both will die. Therefore, it is not only justifiable but also my duty to kill one that the other may live. You would perhaps recoil from the exercise of any such duty and say to yourself: By what authority have I become the arbiter of life and death in human affairs? Man has a right and a duty to use his own life to good purpose, but no right to do away with himself or kill another human being.

But one might say: In regard to the child and the mother, the life of the mother is of so much more value than that of the child, and so the figure of the men struggling for the life preserver is not an appropriate comparison. But who can look into the future and say the life of a child is of so much less value than that of its mother? And suppose you say that one of the men in the water was a worthless tramp and the other a gentleman of importance, would you be justified in shooting the tramp in order to save the life of the gentleman?

A physician has a clear duty to preserve human life, but by what principle can one demonstrate that he is the arbiter of life and death and can therefore decide to kill one human being in order that another may live?

When we approach the consideration of the rights of one human being over the life of another, we are confronted with a problem where the principles we may enunciate may have consequences that will soon extend much further than we think, and lead to results that we would abhor.

Have the parents a right to say whether or not a child shall live and, if so, is it lawful for the physician to act as their executioner when they decide that, all things considered, it is better for the child to die?

If the parents have this right, is it also to be conceded to the state and, if so, under what circumstances? The modern state claims a right over the child higher than that of the parents, a claim which in our

United States has been denied by the Supreme Court.[15] But some countries have already reverted to a condition in which the will of a dictator can at any time decide who is to live and who must die. And there are those in our own country, a small minority let us hope, who would cast off our ancient principles of law and order and set up instead a regime which no longer recognizes the solid foundations of American liberty, but subjects the individual to the whims of a dictator.

In these days, therefore, it becomes a supreme duty to reaffirm the dignity of the human person, who has a right to life, liberty, and the pursuit of true happiness, of which he cannot be deprived except as a punishment for heinous crime of which he has been convicted by due process of law.

REFERENCES

(1) Quoted by *Cheney, Clarence O.:* J. A. M. A. **103:** 1914, 1934, from *Hirst, B. C.:* A Textbook of Obstetrics, Philadelphia, 1906. Cheney says: "This statement by Hirst is quoted as one setting forth, in my opinion, the fundamental principles to be considered in therapeutic abortion." (2) *De Lee, Joseph B.:* The Principles and Practice of Obstetrics, ed. 6, 1933, p. 1112. (3) Philadelphia, 1937, p. 176. (4) *Moore, T. V.:* Principles of Ethics, Philadelphia, 1937, pp. 177-178. It is worth mentioning here that a child may develop normal mentality after the whole left hemisphere was lost as a result of traumatic porencephaly, having its origin in a fall from a window when three years of age. *Kopp, J.:* Deutsche. Ztschr. f. Chir. **116:** 226, 1912. (5) *Bouscaren, T. Lincoln:* Ethics of Ectopic Gestation, Chicago, 1933. (6) *Fitzgerald:* Am. J. Obst. & Gynec. **29:** 53, 1935. (7) *Fritz Schultze-Rhonot and Karl Hansen:* Ergebn. d. ges. Tuberk.-Forsch. 3: 344, 1931. (8) *Fovassier, A. P. H.:* L'avortement medicalement provoqué chez la femme atteinte de tuberculose pulmonaire chronique (thèse), Paris, 1936. (9) *Mcneile, Lyle G.:* J. A. M. A. **103:** 548, 1934. (10) *Cheney:* J. A. M. A. **103:** 1918, 1934. (11) *Taussig, Frederick Joseph:* Abortion Spontaneous and Induced, St. Louis, 1936, p. 386. (12) *Op. cit.*, p. 414. (13) *Haugwitz, Elfriede:* Über die Morbidität und Mortalität bei Kuenstlicher Schwangerschaftsunterbrechung. (Diss. Königsburg) 1935, p. 5 reports 4 deaths in 244 cases, and 23 in which the basic disease was aggravated. (14) *Taussig, Frederick J.:* Abortion Spontaneous and Induced, St. Louis, 1936, The C. V. Mosby Co., p. 414. (15) *Pierce:* Governor of Oregon, et al. *v.* Society of Sisters, 268 U. S., 510.

Catholic University of America

Edwards, Mary S.: Premarital Examination Laws in Operation, J. Soc. Hyg. **26:** 217, 1940.

Premarital Examination laws requiring syphilis tests to be made on both parties have now been in operation for periods ranging up to four years (Connecticut, Jan. 1, 1936). Thus data of considerable importance and interest are beginning to be collected.

Reports of over 600,000 blood tests received from 13 states show an incidence of 1.4 per cent positive for syphilis. A very high percentage of these infected persons (75 to 90 per cent) were unaware of their infection. In one state, in which the premarital examination law has been operating for several years, the number of babies reported as born with congenital syphilis has dropped 50 per cent.

The 20 states now requiring that both parties to a marriage license have a premarital examination for syphilis comprise between 50 and 60 per cent of the population of the country. Statistical calculations suggest that 1 in 35 marriages is endangered by syphilis.

Hugo Ehrenfest.

THE COINCIDENCE OF TUBERCULOSIS OF THE ENDOMETRIUM WITH TUBERCULOSIS OF THE LUNG*

JULIUS E. LACKNER, M.D., WALTER SCHILLER, M.D., AND ALEX S. TULSKY, M.D., CHICAGO, ILL.

(From the Departments of Obstetrics and Gynecology of the Michael Reese Hospital and the Department of Pathology of the Cook County Hospital)

DURING the past year, we have studied the endometrium in a group of women suffering from pulmonary tuberculosis in the tuberculosis division of the Cook County Hospital. Our aim was to determine what, if any, effect a pulmonary tuberculosis has upon the endometrium. It appears that tuberculosis of the endometrium is almost impossible to diagnose clinically. One of us (W. S.) has observed that of many thousands of curettings submitted to pathologists in the course of twenty years, a case of tuberculous endometritis has never been sent in with a diagnosis of this condition made by the clinician.

The literature is replete with case reports of tuberculous endometritis. Daniel reports a case of tuberculosis of the uterine body with no adnexal involvement. Ferroni describes a similar case occurring in an 18-year-old nullipara, the presenting complaint being metrorrhagia. Simon, Cullen, Williams, Diethelm, Heinrich, and Reinhart likewise cite cases of tuberculous endometritis unassociated with adnexitis. Bungeler reports the appearance of an acute miliary tuberculosis following curettage for a tuberculous endometritis, and warns against such a procedure in these cases lest a similar mishap occur. Reinhart adds that the lesion may be primary or secondary, the latter being the more common of the two. Histologically, they differ in that the primary type appears as a small, discrete, sharply-defined lesion composed almost exclusively of epithelioid cells, with involvement of regional lymph nodes. The secondary type is usually greater in area, less sharply-defined, variable in component elements, and does not heal readily. Dickinson is of the opinion that infection of the uterus takes place through the blood stream from a distant focus, through the lymphatics from an adjacent focus, or by direct extension.

The general impression is confirmed that no curettings are sent to the pathologist with the clinical diagnosis of tuberculous endometritis. Some of these cases suggest a chronic adnexitis, or, even more frequently, some disturbance of the menstrual cycle, and in most cases the diagnosis is made only (1) after a curettage, (2) after examination of the removed organs, or (3) upon autopsy. While the majority of lesions appear in the age group of 16 to 36 (Reinhart and Moore), Biggs has reported a case of tuberculous endometritis in a 20-month-old infant (as an exception to the above).

Clinically, two groups of tuberculous endometritis may be distinguished. First, the involvement associated with progressive tuberculosis of the ovaries, the tubes, or both, the endometritis representing only an associated pathologic process of minor clinical importance. Second, tuberculosis of the endometrium with normal tubes and ovaries, associated with and developing from a tuberculous infection of an organ outside of the pelvis, as for example, the lungs, and the mesenteric or hilar lymph nodes, this representing an important and obviously unsuspected syndrome of primary extragenital tuberculosis.

*Presented at a meeting of the Chicago Gynecological Society, April 19, 1940.

This latter group comprised the special and specific condition in which we became interested. We attempted to find out how often women with a primary progressive tuberculosis of the lungs would show an isolated clinically latent tuberculosis of the endometrium. Consequently, in this study, we eliminated women with tuberculosis of the lungs and associated manifest, chronic, probably tuberculous inflammation of the adnexa, and have examined only women with evident progressive tuberculosis of the lungs, and with no clinically manifest inflammatory process of the ovary or tube. Our material consists of 134 biopsies obtained from 125 female patients in the tuberculosis division of the Cook County Hospital, the entire group showing radiologic and laboratory evidence of active pulmonary tuberculosis. In each of these women endometrial strips were obtained, using the suction curet described by Randall. There is no question that occasionally the amount of tissue obtained is so small that pathologic analysis furnishes meager information. Consequently, only positive findings should be accepted for final conclusions; negative findings have no necessary significance. However, it may be expected that an endometrium which is active throughout, soft and proliferating, or which is in the process of developing multiple tuberculous nodes, would give evidence of its physiologic or pathologic characteristics even though, by suction curettage, but a small piece of tissue is obtained. Rock, in a recent study involving the role of endometrial biopsy in diagnosis, has found four, apparently latent, cases of tuberculosis of the endometrium.

With this restriction borne in mind, then, it may prove of interest that we found in the 125 women only two cases of manifest endometrial tuberculosis. The histories of these cases are as follows:

CASE 1.—M. K. (Hosp. No. 360-1233, 265), a 39-year-old colored female, was admitted to Cook County Hospital on Jan. 12, 1939, with the complaints of malaise, weakness, and cough of three weeks' duration. She had been in a poor state of health (severe secondary anemia) for the past twelve years. Present illness was ushered in by an upper respiratory infection characterized by marked weakness and expectoration of a whitish phlegm.

Past history was essentially negative except for the usual childhood diseases. The menarche had occurred at 13 years, every 28 to 30 days, of five days' duration; flow moderate; no pain. Amenorrhea had been present from birth of her last baby in May, 1938 to January, 1939. Patient was a gravida v, para vi. There was one set of twins. Her oldest child was 17 years of age. Last menstrual period occurred on Jan. 2, 1939.

Family history was essentially negative. Inventory by systems likewise was negative.

Physical examination revealed a poorly nourished adult female. Temperature was 101.8° F., pulse 108, and respiration 27. Lungs showed increased tactile and vocal fremitus on left side with decreased resonance. There were moist râles through entire left chest with patch of cavernous breathing posteriorly. Heart and abdomen were negative. Pelvic examination showed a parous introitus, and relaxed pelvic floor. The vulva and vagina were negative. There was a moderate cystorectocele; the corpus erect and of normal size; adnexa not palpably enlarged, fixed, or tender; cervix appeared normal.

X-ray examination of the chest on Jan. 13, 1939, was diagnostic of a tuberculous pneumonic consolidation of the left chest; tuberculosis organisms were recovered from the sputum, and patient was transferred to the Tuberculosis Hospital, where

a diagnosis of far-advanced bilateral pulmonary lesion was made. Her weight was 84 pounds. Serology was negative, white blood count, 7,200, red blood count 3,900,000. Hemoglobin 70 per cent. Urine negative. Sputum persistently was positive. No therapy could be carried out. Endometrial biopsy was obtained Jan. 26, 1939, and biopsy of the endocervix on Feb. 15, 1939. There were no pelvic complaints at any time.

Fig. 1.

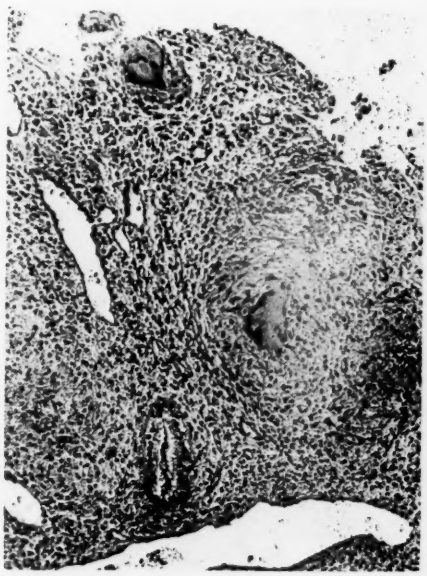


Fig. 2.

Fig. 1.—(Case 1.) Endometrium from suction curettage. Numerous small tubercle nodes, most of them with typical Langhans' giant cells. Magnification ×60.

Fig. 2.—(Case 2.) The same section as in Fig. 1 under higher power.

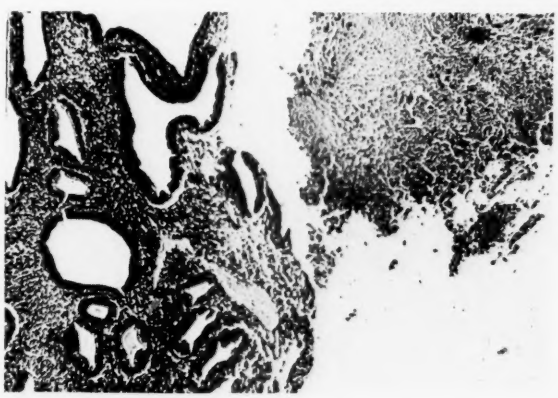


Fig. 3.—(Case 2.) Endometrium from suction curetting. Left side, cystic hyperplasia. Right side, small caseating tubercle in the cytogenic tissue. Magnification ×60.

CASE 2.—M. S. (Hosp. No. 360-1233, 83), a 43-year-old white female, para iii, gravida iii, was admitted to the tuberculosis division of Cook County Hospital on June 2, 1939, with complaints of cough, expectoration, weight loss, weakness, and dyspnea of four months' duration. This was initiated by a severe cold characterized by hemoptysis over a period of several weeks, and marked weakness.

Past history: She had diphtheria when a child. Menses began at 13 years of age, irregular every four to six weeks, of two days' duration, flow scanty, no pain. Cervical amputation for cystic hypertrophic cervix was done in 1935. Last menstrual period occurred on May 20, 1939.

Family history was negative.

Inventory by systems was essentially negative.

Physical examination revealed a poorly nourished adult female. Temperature 97.2° F., pulse 84, respiration 24. Head and neck were negative. X-ray picture revealed infiltrative changes throughout both lungs, most pronounced in the upper halves, with bilateral cavitation. Remainder of general examination was negative. Pelvic examination was as follows: Parous outlet with relaxed floor; slight cystorectocele; corpus uteri in retroversion but not fixed. The adnexa were freely movable and normal; cervix not present (removed by operation). Sputum was positive for *B. tuberculosis.* White blood count was 8,200, red blood count 3,870,000. Hemoglobin 70 per cent. Urine negative. Serology negative. Weight varied from 100 to 80 pounds in course of illness. No therapy was carried out. Endometrial biopsy was obtained June 16, 1939.

DISCUSSION

It can be seen by the protocols of the above cases that the history and clinical findings resemble to a large extent the history and clinical findings of most of the cases of tuberculous endometritis gleaned from the literature. That is, they are characterized by an extreme paucity of leading pelvic symptoms and of clinical and laboratory findings. Both patients apparently had normal or almost normal menstrual cycles. They had no gynecologic complaints and by the same token vaginal examination was completely negative in one case and elicited minimal findings in the second case. Neither of these cases had a vaginal discharge. This instance of two cases among 125 corresponds to an incidence of about 1.60 per cent. This harmonizes with the figures obtained from the autopsy records of the Cook County Hospital during the last ten years. In this period of time about 13,000 autopsies have been performed. Roughly, three thousand of these were done on adult women. Of this group, 113 had pulmonary tuberculosis. In the 113 cases there were two instances of tuberculous endometritis without adnexitis (1.77 per cent). There were two cases of tuberculous adnexitis and associated tuberculous endometritis (1.77 per cent). There were six cases of tuberculous salpingitis (5.31 per cent), and hence four cases of tuberculous adnexitis without tuberculous endometritis. Among 107 cases of women with tuberculosis of the lung without tuberculosis of the adnexa there were two cases of isolated tuberculous endometritis. There were then 1.87 per cent of cases of isolated tuberculous endometritis in the autopsy material as compared with 1.60 per cent in our clinical material.

From the pathologic point of view we may use the classification which Ghon has given for the genesis of genital tuberculosis in women. Tuberculosis of the endometrium, according to its localization, never is a primary condition. In secondary tuberculosis with (1) endogenous spread we must distinguish between (a) a generalization of the infection, with the local tuberculosis representing only a part of the generalized infection or (b) an isolated hematogenic focus or metastasis. The second type of secondary tuberculosis (2) has been called by Ghon "reinfection," represented by cases of a new infection in some other organ after the organism has developed a primary focus in one organ. Pozzi called

this type of reinfection "primitive secondary tuberculosis" and differentiated between reinfection developing from the organism itself and a reinfection from the outside. Tuberculosis of the endometrium, in our cases, must be classified as secondary tuberculosis of the Type b. It represents not the part and component of a generalization, as in a miliary tuberculosis, but an isolated metastasis, so to speak, of the primary pulmonary process. So far as the method of spread is concerned, by exclusion we must accept the hematogenic route. It may be similar to the spread of a miliary tuberculosis, the difference being that the tubercle bacilli circulating throughout the organism found a favorable nidus only in the endometrium. Ghon quoted as an example of this type of secondary tuberculosis, hematogenic salpingitis. The possibility of the occurrence of an isolated hematogenic tuberculous endometritis would appear to be proved by our findings.

We wish to take this opportunity to thank Dr. Mendelssohn for permitting us to use the patients on his service in the tuberculosis division for this study.

REFERENCES

(1) *Biggs, G. P.:* Proc. N. Y. Path. Soc., p. 259, 1901. (2) *Bungeler, W.:* Frankfurt. Ztschr. f. Path. **47:** 313, 1935. (3) *Cullen, T. S.:* Johns Hopkins Hosp. Rep. **4:** 1894-1895. (4) *Daniel, C.:* Rev. franç de gynéc et d'obst. **20:** 305, 1925. (5) *Idem:* Ibid. **24:** 220, 1929. (6) *Idem:* Gynéc. et obst. **11:** 161, 1925. (7) *Depkin, H.:* The Menstrual Cycle in Tuberculous Adnexitis, and a Discussion of the Pathogenesis of Uterine Tuberculosis, Inaug. Diss. Rostock, 1920. (8) *Dickinson, A.:* Am. J. Surg. **11:** 558, 1931. (9) *Diethelm, M. W., and Ramsay, T. L.:* Am. J. Obst. & Gynec. **30:** 420, 1935. (10) *Ferroni, E.:* Zentralbl. f. d. ges. Geburtsh. u. Gynäk. **2:** 19, 1924. (11) *Fruhinsholz and Feuillade:* Gynéc. et obst. **10:** 305, 1924. (12) *Gerich, Obokar:* Monatschr. Geburtsh. u. Gynäk. **70:** 278, 1925. (13) *Ghon, A.:* Wien. med. Wchnschr. 44 & 45, 1922. (14) *Idem:* Genesis of Genital Tuberculosis in Women. Vorträge des Ersten Arztlichen Special Kurses für Frauen u. Herzkrankheiten in Franzenbad, September, 1922. (15) *Gragert, Otto:* Beitr. z. klin. d. Tuberk. **63:** 768, 1926. (16) *Gummert:* Monatschr. f. Geburtsh. u. Gynäk. **17:** 1242, 1903. (17) *Hartmann-Keppel, G. L.:* Gynéc. et obst. **8:** 347, 1923. (18) *Heinrich, A.:* Am. J. Obst. & Gynec. **23:** 579, 1932. (19) *Hussy, P., and Vetter, H.:* Schweiz. med. Wchnschr. **56:** 162, 1926. (20) *Kundrat:* Arch. f. Gynäk. **65:** 87, 1912. (21) *Mayer, A.:* Beitr. z. d. Tuberk. **63:** 874, 1926. (22) *Reinhart, G. L., and Moore, R. A.:* J. Lab. & Clin. Med. **14:** 413, 1929. (23) *Reeb:* Bull. Soc. d'obst. et de gynéc. **14:** 267, 1925. (24) *Rock, J.:* Am. J. Surg. **48:** 228, 1940. (25) *Schroder, R.:* Monatschr. f. Geburtsh. u. Gynäk. **55:** 15, 1921. (26) *Schroder, R.:* Nordwest-deutsche Ges. f. Gynäk. u. Geburtsh. **2:** 10, 1920. (27) *Simon, Felix:* On the Symptoms of Open Uterine Tuberculosis, Inaug. Diss. Giesen, 1920. (28) *Schellenberg:* Zentralbl. f. Gynäk. **56:** 2105, 1932. (29) *Schlimpert:* Arch. f. Gynäk. **94:** 867, 1922. (30) *Stewart, C.:* J. Obst. & Gynaec. Brit. Emp. **40:** 299, 1933. (31) *Schroeder, E.:* Deutsche med. Wchnschr. Leipzig and Berlin 1903, 29 Ver.-Beil., 138. (32) *Franque, V.:* Prag. med. Wchnschr. **50:** 653, 1906. (33) *Williams, P. R.:* Am. J. Obst. & Gynec. **6:** 230, 1923. (34) *Weibel, W.:* Tuberculosis of the Female Genital Apparatus, Halban-Seitz. **5:** pp. 329 and 353.

DISCUSSION

DR. CHARLES E. GALLOWAY.—My knowledge of tuberculous endometritis is purely academic, and I do not consider myself an authority because I have had no experience with it. It seems to me that this subject opens up a very interesting field of research that so far has not been covered. If these patients in the various county institutions who are suffering from tuberculosis can be used for investigative purposes without harm to the individual patient, I believe we are justified in doing so. No one knows anything about the early stages of tuberculous endometritis as the authors have described it.

I should like to emphasize one of the points brought out, namely that negative findings are of no value, although positive findings are of some importance. Evi-

dently the authors have segregated a group of patients suffering from tuberculous lesions and investigated the endometrium; and from their report we assume that in patients without palpable adnexal swelling, we can find tuberculous lesions in the endometrium in about one out of fifty or sixty. A question which comes to my mind is: What happened later to these 134 patients after the diagnosis had been made? Suppose we made a positive diagnosis of tuberculous endometritis, what are the results of the disease? What goes on following the discovery of the tuberculous endometritis and what is done with the patient? Does the infection spread from the endometrium to the adnexa or has it come from the adnexa to the endometrium? I do not believe that any one has much knowledge concerning these things.

This thesis has also brought up the question, Do we as gynecologists have a right to inspect these tissues? What about the other specialists and what will happen to the patients in our institutions? I think we will have to be cautious about going too far.

DR. A. G. GABRIELIANZ.—I would like to ask if the von Pirquet test was used in cases of primary tuberculosis of the internal genital organs? Was the diagnosis confirmed by operation?

DR. WALTER SCHILLER.—The cases of so-called tuberculosis of the cervix were discovered by direct inspection through a speculum, and I do not know whether a von Pirquet test was done.

The textbooks generally mention two types of tuberculosis of the endometrium only, one in which the tuberculosis of the endometrium is associated with a tuberculosis of the tube and eventually of the ovary, and the second in which the tuberculosis of the endometrium is part of a generalized hematogenic tuberculosis. Our cases deal with a localized hematogenic tuberculosis of the endometrium which evidently did not produce local symptoms.

DR. J. P. GREENHILL.—Dr. Galloway's facetious remarks may lead us to believe that the work of Dr. Lackner and his associates has only a theoretical interest because, even if women with active pulmonary tuberculosis have endometrial tuberculosis, nothing will be done about it. It seems to me that the reverse of this question is important. As gynecologists, we are interested in knowing how many women with genital tuberculosis have pulmonary tuberculosis at the same time.

My interest in this subject is more than academic, because many years ago I studied 200 cases of proved genital tuberculosis. In this series at least 25 per cent of the women had pulmonary tuberculosis. The actual incidence of pulmonary involvement was undoubtedly higher.

In my series of 200 cases of genital tuberculosis, the tubes were involved in all the cases and the uterus in more than 70 per cent. The generally accepted impression is that nearly all cases of tuberculous endometritis are secondary to tubal tuberculosis. As Dr. Schiller has suggested, in rare cases the tuberculous endometritis may be primary and the tubal infection secondary.

CONCENTRATION OF PARALDEHYDE IN THE BLOOD FOLLOWING ITS ADMINISTRATION DURING LABOR*

HERMAN L. GARDNER, M.D., HARRY LEVINE, PH.D., AND MEYER BODANSKY, PH.D., M.D., GALVESTON, TEXAS

(From the Departments of Obstetrics and Gynecology and Pathological Chemistry, University of Texas School of Medicine, and the John Sealy Memorial Research Laboratory)

PARALDEHYDE for producing analgesia and amnesia in obstetric deliveries was introduced by Rosenfield and Davidoff[1] in 1932. Since then many reports have been published concerning the value of this drug, when given either alone or in combination with other drugs, such as benzyl alcohol, sodium pentobarbital, morphine, sodium amytal, and ether. A review of these contributions is not essential in this connection in view of the summary of the literature by Bushnell.[2] Here it suffices to state that paraldehyde appears to be a comparatively safe drug as regards both mother and fetus.[3, 4] However hypersusceptibility to the compound has been encountered,[5-7] and in two known instances[5, 7] the result was fatal.

Owing, possibly, to the relative infrequency of untoward effects, little attention has been given to this aspect of the problem, so that the use of paraldehyde is, in some respects, still empirical. Thus, we find no published data concerning the concentrations of paraldehyde in the blood following its administration to subjects in labor. Such data may be expected to be of value in defining the concentrations required to produce a desired degree of amnesia and analgesia and in indicating deviations in the metabolism of paraldehyde associated with certain complications, such as eclampsia and liver disease.[8] It is to be realized that the effect of a given dose of paraldehyde may be quite variable in different individuals.

In view of these circumstances it seemed desirable to investigate the concentrations of paraldehyde present in the blood of parturient women at intervals following administration of the drug. The present report is based on the results in 20 patients who were given a single dose of 30 c.c. of paraldehyde in 60 c.c. of olive oil. In our experience the use of olive oil lowered the rate of absorption and assured a more prolonged effect. Ten of the patients received the drug by rectal injection; the others were given the paraldehyde-olive oil mixture by the nasal tube route. The paraldehyde was administered when the cervix showed a dilatation of approximately 3 cm., or more, and when forceful contractions were occurring at intervals of about three to five minutes. Patients who either expelled or vomited a portion of the drug have not been included in this report.

*This work was supported partly by a grant from the Committee on Therapeutic Research (No. 383), Council on Pharmacy and Chemistry, American Medical Association.

To make possible even a rough evaluation of the effect of paraldehyde, other types of medication, such as morphine or barbiturates, were excluded. However, the majority of patients required an anesthetic during delivery. Nitrous oxide was used in most instances, novocaine (local or caudal) in several cases, and chloroform in one case. Ether was not used, as its presence in the blood would have interfered with the determination of paraldehyde.

In collecting the blood specimens a necessary precaution is to avoid the use of alcohol sponges in cleansing the arm. Alcohol, like ether and acetone, is a volatile oxidizable substance and interferes, therefore, with the determination of paraldehyde. Cotton sponges moistened with mercury bichloride solution were employed instead.

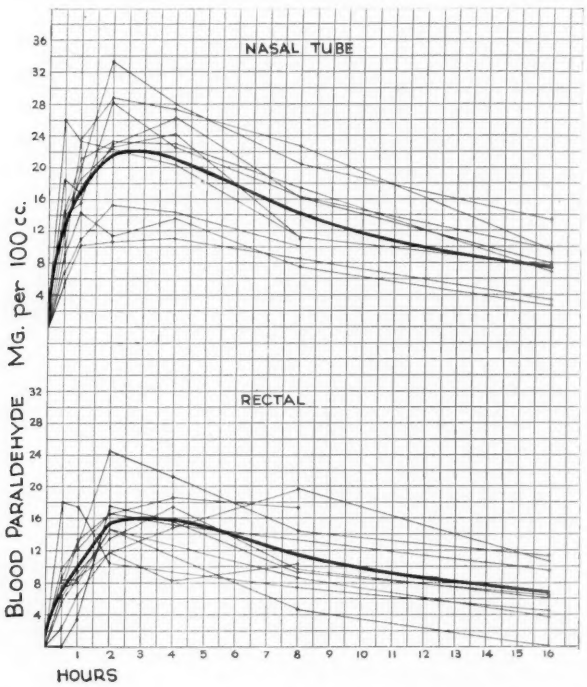


Fig. 1.—Concentrations of paraldehyde in the blood following its administration in patients during labor. Dose: 30 c.c. of paraldehyde in 60 c.c. of olive oil. Thin lines represent individual cases. Heavy lines represent average values obtained following rectal and gastric (nasal tube) administration, respectively.

PROCEDURE

The routine procedure consisted in obtaining a specimen of blood for a blank determination immediately before administration of the paraldehyde, and additional specimens at ½, 1, 2, 4, 8, and 16 hours after administration. Oxalate was used as anticoagulant. A sample of cord blood was obtained in most instances. All specimens were kept in tightly stoppered vials in the refrigerator until ready for analysis by the method of Levine and Bodansky.[9]

RESULTS

The results are represented by the two sets of curves in Fig. 1. From these curves it is seen that individual variations were marked, but that, in general, the

concentrations of blood paraldehyde were higher when the drug was given orally than when given rectally. A comparison of the curves representing the mean values (heavy lines) shows that the maximum concentrations of paraldehyde in the blood following rectal administration were on the average 70 to 75 per cent of the values obtained following oral administration.

As shown in Fig. 1, the highest maximum level for the 10 individual curves in the "rectal" group was 24.4 mg. per cent. In this case the patient had complete amnesia for seven hours, the amnesia beginning about twenty minutes after administration of the paraldehyde and lasting until two hours before delivery. The lowest maximum level for this group was 11.8 mg. per cent. In this case, the patient experienced no amnesia, although the pains were much relieved.

The highest and lowest maximum concentrations obtained by the "nasal tube" (oral) method were 33.2 and 11.0 mg. per cent, respectively. The patient with the high blood paraldehyde curve experienced complete amnesia for ten hours, delivering five and one-half hours following administration without requiring any other anesthetic. On the other hand, the patient with the low paraldehyde curve obtained little or no amnesia, though her pains were apparently lessened. She delivered, under local anesthetic, five and three-fourths hours following administration of the paraldehyde. The remaining 8 patients in this group experienced complete amnesia for periods varying from four and one-half to eleven hours.

Of the 10 patients who received the drug by the rectal route, 6 experienced a period of complete amnesia, varying from two to ten hours, the average being six hours. Three patients, with maximum blood paraldehyde levels of 11.8, 14.5, and 19.7 mg. per cent, respectively, experienced no amnesia. One patient with a maximum blood level of 17.5 mg. per cent had partial amnesia.

No patient in either group in whom the blood paraldehyde concentration rose to 20 mg. per 100 c.c., or above, failed to experience a period of complete amnesia. However the possibility is recognized that the level of consciousness is quite variable and that in some individuals a higher concentration than 20 mg. may be required to produce amnesia. One such case has been encountered since completing the present series of observations.

Where complete amnesia occurs, the onset is usually within fifteen to thirty minutes after the drug is given. This is of interest in view of the observation that the blood paraldehyde level at thirty minutes was frequently lower than later when the amnesia had been abolished. Almost invariably the concentration at the end of the period of amnesia was higher than at the beginning of amnesia. These relations are at present under investigation, the working hypothesis being that a high concentration of paraldehyde is attained in the brain soon after absorption of the drug begins and that this determines the onset and degree of narcosis. In view of the solubility of the drug in lipoids, it may be assumed that its distribution between the blood and tissues is such that large amounts accumulate in organs such as the brain and liver which are rich in lipoid material. As the concentration in the brain diminishes, the narcotic effect disappears.

The concentration of paraldehyde was determined in 13 specimens of cord blood. In two instances blood was obtained simultaneously from the mother. The results in these cases, cases 1n and 3r, are included in Table I. In the other instances, it was necessary to derive the values for the concentration in the maternal blood at the time of delivery by referring to the respective blood paraldehyde curves. The data thus obtained are likewise given in Table I. It will be noted that in the majority of instances the values for cord and maternal blood were in fairly close agreement. The averages for the entire group were: 15.5 mg. per cent for cord blood; 16.6 mg. per cent for maternal blood.

In passing it may be noted that the three infants in our series with the highest cord blood paraldehyde values (24.1, 24.4, 27.2 mg. per 100 c.c.) exhibited no unusual symptoms; none showed the slightest degree of apnea. Delivery in these cases occurred without other anesthesia. Apnea was observed in three other infants (two of these were premature) in whom the cord blood paraldehyde amounted

to 8.8 to 12.6 mg. per 100 c.c. In one instance the mother received nitrous oxide anesthesia; in the others a local anesthetic was used. No delay in respiration was observed in four other infants in our series, with cord blood values of 8.8 to 11.8 mg. per 100 c.c., and who were delivered without anesthetics. Kotz and Kaufman[4] investigated the effect of paraldehyde analgesia on the onset of respiration and found this to be definitely delayed. The average for 100 babies whose mothers received paraldehyde was 39.5 seconds, compared to an average of 9.8 seconds for a similar group whose mothers received no analgesia. This slight delay in initial respiration was not considered to have any injurious effect on the baby (see also Colvin and Bartholomew[3]).

TABLE I. CONCENTRATIONS OF PARALDEHYDE IN CORD BLOOD AND MATERNAL BLOOD AT DELIVERY

PATIENT	CORD BLOOD MG. PER 100 C.C.	MATERNAL BLOOD MG. PER 100 C.C.
1n*	27.2	28.8
3n	24.4	25.2
5n	24.1	26.7
6n	11.8	11.0
7n	12.6	12.6
10n	17.8	21.0
1r	18.7	15.6
2r	8.8	12.0
3r	7.7	8.3
4r	9.6	14.5
6r	12.3	13.8
7r	14.2	13.9
8r	8.8	12.6
Averages	15.5	16.6

*n, denotes that the paraldehyde was given by nasal tube; r, that it was given rectally.

SUMMARY

The concentration of paraldehyde in the blood was determined in parturient women at intervals (½, 1, 2, 4, 8, and 16 hours) following rectal, or oral (nasal tube) administration of 30 c.c. of paraldehyde in 60 c.c. of olive oil.

The highest and lowest maximum concentrations attained in 10 patients who received the drug rectally were 24.4 and 11.8 mg. per cent, respectively. Six of these subjects experienced a period of complete amnesia, varying from two to ten hours.

In 10 patients who received the drug orally, the highest and lowest maximum concentrations were 33.2 and 11 mg. per cent, respectively. The patient with the highest blood paraldehyde curve experienced complete amnesia for ten hours. The patient with the lowest curve experienced little or no amnesia, although her pains were lessened.

All patients in whom the blood paraldehyde rose to 20 mg. per 100 c.c., or above, and some who did not attain this level, experienced a period of complete amnesia.

Analyses of 13 cord blood specimens revealed that at the time of delivery the concentration of paraldehyde in the fetal circulation approximated that in the maternal blood. The averages for the entire group were: 15.5 mg. per cent for cord blood; 16.6 mg. per cent for maternal blood.

REFERENCES

(1) *Rosenfield, H. H., and Davidoff, R. B.:* New England J. Med. **207:** 366, 1932. (2) *Bushnell, L. F.:* Internat. Abst. Surg. **67:** 155, 1938. (3) *Colvin, E. D., and Bartholomew, R. A.:* Internat. Clin. **4:** 191, 1938. (4) *Kotz, J., and Kaufman, M. S.:* J. A. M. A. **113:** 2035, 1939. (5) *Kotz, J., Roth, G. B., and Ryon, W. A.:* J. A. M. A. **110:** 2145, 1938. (6) *Jinkins, J. L., and Herrod, J.:* Bull. John Sealy Hospital and University of Texas School of Medicine **1:** 27, 1939. (7) *Stiles, J. A.:* Personal communication to M. B. (8) *Bodansky, M., Jinkins, J. L., and Levine, H.:* (In press.) *Levine, H., Gilbert, A. J., and Bodansky, M.:* J. Pharmacol. & Exper. Therap. **67:** 299, 1939; *Idem:* Ibid. **68:** July, 1940. (9) *Levine, H., and Bodansky, M.:* J. Biol. Chem. **133:** 193, 1940.

PELVIC TUBERCULOSIS

With a Report of a Case of Tuberculosis of the Cervix

A. H. Lahmann, M.D., F.A.C.S., and S. F. Schwartz, M.D.,
Milwaukee, Wis.

(From the Gynecological Service of the Milwaukee County General Hospital and Department of Obstetrics and Gynecology of the Marquette University School of Medicine)

TUBERCULOUS involvement of the female genitalia, although seemingly rare, is more prevalent than is generally assumed. The increased number of articles appearing in the literature has, in recent years, made for a much better understanding of his subject by the profession. However, few men have had enough individual experience with a sufficient number of cases to evaluate signs and symptoms as presented by the patient for adequate diagnosis, and treatment, which is still a largely controversial subject, remains a major problem.

Due to the fact that genital tuberculosis has been estimated to constitute from 5 to 8 per cent of all pelvic inflammatory conditions, it has of necessity become one of the important diseases to consider in the differential diagnosis of any affection of the female genitalia. However this is usually very difficult, and may be impossible on occasion, because the symptoms and signs are not typical and closely resemble those of numerous other maladies affecting the female genitalia.

Various investigators have found that genital tuberculosis is usually secondary to tuberculosis elsewhere in the body, and occurs most frequently in the years of active sex life. Also, there is a marked tendency for the disease to descend from the tubes to the endometrium, and it involves most commonly the organs in the order mentioned, namely: (1) tubes 90 per cent, (2) endometrium 75 per cent, (3) ovaries 30 per cent, (4) cervix 5.5 per cent, and vagina and vulva, 0.5 per cent.[1] There is no tendency for the disease to spread to the urinary tract.

MATERIAL

In the preparation of this paper, a study was made of 21 patients with tuberculosis involving the female genitalia. These patients were admitted and treated at the Milwaukee County General Hospital in the eleven-year period from January, 1929 to January, 1940. Of the cases

reviewed, positive evidence for the diagnosis of genital tuberculosis could not be obtained in 6 instances, because no tissue was available for microscopic examination.

Several of these patients came to us after a gynecologic operation elsewhere with the complaint of a draining sinus from an old surgical scar in the lower abdomen, and with a diagnosis of tuberculous peritonitis. Some were operated upon at our hospital, but at the time of operation, due to the fact that the genitalia together with a portion of the peritoneal cavity were involved by some indefinite infection, only a small section of omentum or peritoneum was removed for biopsy, which was reported later by the pathologist to be tuberculosis.

Because there is lack of definite proof by biopsy as to the existence of tuberculosis of the genitalia in these 6 cases, they have been excluded from this report and only the remaining cases, 15 in number, have been analyzed for presentation here.

All of our patients were in the "childbearing age" group. Twelve of the 15 (80 per cent) occurred in women between the ages of 20 and 30, two between the ages of 31 and 35, and the remaining patient was 43 years old. However, it is felt that the average age should be lowered considerably since all of the patients undoubtedly had been afflicted with tuberculous involvement of the genitalia before its discovery by surgical intervention. Many of the patients attending our outpatient department clinic had gynecologic complaints long prior to operation, and these complaints, we feel, if properly interpreted would have led to an earlier diagnosis.

A history of menstrual disturbance as described by some writers was not a significant factor in our study. The only finding considered of some value was the disclosure that 6 of the series, or 40 per cent, had begun to menstruate between the ages of 15 and 17 years, which is somewhat later than the average. The onset of menses in the remaining patients was earlier, one beginning at eleven years of age.

Four, or approximately 26.5 per cent, were sterile, although only one of these actually complained of sterility. Two others gave a history of one pregnancy with early abortion. Three of the series were single while 6 had families ranging from one to six children.

Various investigators have reported the existence of pulmonary tuberculosis in from 50 per cent to 90 per cent of patients with genital tuberculosis examined at autopsy.[2] On the other hand, King[3] in a review of 26 cases of pelvic tuberculosis, points out that only 6 of his series showed evidence of pulmonary involvement and states that "it is clear that the extent of pulmonary involvement plays at most but a small part." This is definitely in keeping with our findings, in that 12 of the 15 cases reported in this paper had negative chest x-rays or were considered chest-negative clinically. Only 3 showed signs of pulmonary tuberculosis.

Very enlightening is the fact that in not even one instance was the diagnosis of genital tuberculosis correctly made or even considered preoperatively, the usual diagnosis being tuboovarian abscess, acute or chronic salpingo-oophoritis, pelvic cellulitis, appendicitis, etc. More important still is the disclosure that in only one case of the entire series was the diagnosis made by the operating surgeon visualizing the gross pathology, the others being diagnosed microscopically.

The symptoms of tuberculous involvement of the female genitalia resemble closely those of chronic gonorrheal salpingitis. Pelvic examination is of very little assistance in differential diagnosis unless the patient is a virgin, in which case pelvic inflammation is a clue to the possible

involvement of the genitalia with tuberculosis, since no other cause for the infection can be ascertained. The two most common complaints were pain in the lower abdomen confined to one or both sides, and vaginal discharge, usually of long standing. A record of the various other symptoms encountered, in their order of frequency, were weight loss, urinary distress, vomiting, weakness, cough, abdominal mass, fever and chills. We believe, however, that these symptoms offer little value from the standpoint of differential diagnosis, since they are often encountered in many other acute and chronic ailments involving the pelvis and abdomen.

Eight patients of this series are alive and well, including one on whom a right salpingo-oophorectomy was performed in 1930 when the patient was 27 years old. We were unable to contact four patients, and therefore have no information as regards their present condition. The remaining three are known to be dead; one patient aged 21, died three days following a bilateral salpingo-oophorectomy. Another, aged 25 years, also had a libateral salpingo-oophorectomy followed by a very stormy postoperative course and died approximately four months later. The third patient, a 25-year-old negress with advanced pulmonary tuberculosis, made an uneventful recovery following a bilateral salpingectomy and left oophorectomy, but died of pulmonary tuberculosis six years later.

A very high incidence of immediate postoperative complications was evident. The most distressful of these was draining sinuses from the incision, many fecal in character and of long standing. Eight patients developed sinuses which drained from approximately four months to four years. Six of the surgical incisions healed primarily. The average postoperative stay in the hospital was found to be 43.4 days.

Pelvic tuberculosis may result from one of the following modes of spread: (1) Contiguity, from the soft tissues adjoining the pelvis; (2) lymphogenous, usually from the abdominal cavity; (3) hematogenous, from some distant focus; (4) primary, with direct inoculation by coitus.

The tubes are most commonly involved in tuberculosis of the female genitalia. Glass and Crescí[4] have reported an incidence of 85.5 per cent in their series of 36 cases of genital tuberculosis at the Long Island College Hospital from 1923 to 1937.

Ascending infection from some other portion of the genital tract rarely, if ever, occurs, the infection usually originating from a tuberculous peritonitis with involvement of the perisalpinx or the endosalpinx or both, or from some focus elsewhere in the body. The original focus may heal while the newly formed lesion continues to flourish. Authorities estimate that in fully one-half of the cases of tuberculosis of the tubes, involvement of the endometrium has occurred.

Stevenson and Wharton[5] report tuberculous endometritis in approximately 85 per cent of a series of 402 cases of tuberculous salpingitis collected in forty-seven years at Johns Hopkins Pathology Laboratory.

The supposed high incidence of involvement of the endometrium in tuberculous salpingitis is very important, since in patients with genital tuberculosis, microscopic study of uterine curettings alone would yield a diagnosis in at least 50 per cent of the cases. However, curettement

is considered by some to be a rather hazardous procedure because of the possibility of widespread dissemination of the tuberculous process following the use of the curet.

In our cases, the tubes were involved in 6 patients, the tube and ovary in 4, the ovary in 4, and the cervix in only one instance. This does not exclude the involvement of a greater number of structures, since in many instances the tubes, ovaries, or uteri were not removed and therefore not available for examination.

Since the literature stresses such a high percentage of uterine involvement, it is significant that there was endometrial involvement in not even one case of our series, although 4 uteri were available for careful microscopic examination.

Bishop[6] reports a case of extensive destruction of the tubes and cervix without involvement of the endometrium or myometrium which in this instance tends to show a relative resistance of the endometrium to tuberculous infection. Danforth[7] mentions the fact that Watson, in 1934, reported a similar case.

Tuberculosis of the ovaries is of much less frequency than that encountered in the tubes or uterus. Involvement is estimated at from 15 to 20 per cent of all cases of pelvic tuberculosis. However, involvement occurred in 8 of our cases, or 53.3 per cent, which demonstrated ovarian tuberculosis to be of far greater frequency than that occurring in the endometrium, and corresponds with the findings of Schmitz and Geiger,[8] who place the endometrium after the ovaries in the order of their frequency of occurrence.

In only one case (6.7 per cent) was tuberculosis of the cervix encountered.

Tuberculosis of the cervix was first described in 1831 by Raynaud, and the literature since has contained numerous descriptions, with many authorities[9, 7] reporting isolated cases. Collins[10] in February, 1939, reported on a study of 191 cases available in the literature, 16 of which he considered to be primary tuberculosis of the cervix. A primary tuberculosis of the cervix can be considered only when no other focus of tuberculosis is demonstrable in the patient, and before a case is placed in this category "an exhaustive autopsy should have been performed to exclude the presence of an earlier tuberculous lesion."[2]

Tuberculosis of the cervix is usually associated with tuberculosis elsewhere in the body. Lester[11] states that 4 per cent of women who have tuberculosis elsewhere in the body exhibit this disease of the cervix. It is usually confused with carcinoma, syphilis, severe erosion, gonorrhea, sarcoma, and actinomycosis, and can be diagnosed definitely only by microscopic examination of the four pathologic forms mentioned below, the first two of which are most commonly seen. It seems that this classification really describes the various stages of the same pathologic process.[12]

1. Vegetative, this type surrounds the entire os and consists of a large fungating granuloma, bright red in color, which bleeds very easily.

2. Ulcerative type, which is the most common variety and appears as a large, deep, irregular, punched-out ulcer.

3. Miliary, the cervix has the appearance of implanted miliary tuberculosis.

4. Interstitial, the infection involves the muscle and connective tissue, is hard, swollen, and nodular.

CASE REPORT

Mrs. A. M., a 25-year-old, married, white woman, gravida ii, para ii, children 5 and 1½ years old, respectively, entered the Milwaukee County General Hospital on Feb. 2, 1939. She had been a patient in the hospital on two previous occasions, the first time in November, 1937, seven months after delivery of her youngest child, when

she complained of intermittent radiating right lower abdominal pain which had occurred at intervals for five months. She also complained of menstrual irregularity for the past two months with almost daily bleeding for one month.

Three days prior to admission she began vomiting a greenish purulent material. On the day of admission she stated she had vomited about one-half cupful of blood.

Onset of menses occurred at 17 years, every twenty-eight days for three or four days. There was no menstrual disturbance up to the present illness. Family history was negative.

Examination revealed a well-preserved, 148-pound, white female, not acutely ill. General physical examination was negative except for slight tenderness over McBurney's point on deep palpation.

Vaginal examination revealed a freely movable cervix with third degree retrodisplacement of the uterus; no adnexal masses or tenderness were elicited. The cervix was lacerated and eroded. Laboratory findings were negative, as was the x-ray picture of the chest. The patient signed a release two days after admission.

One and one-half years after the first admission she was readmitted complaining of swelling and pain of five weeks' duration in the right inguinal region and right labia majora. Examination other than that performed by the interne was refused. This revealed a moderate white discharge and a right Bartholin abscess. The cervix appeared hypertrophied and eroded. There was a tender left adnexal mass, while the right side was negative. The right inguinal glands were markedly enlarged, tender, and warm. Cervical smears were positive for gram-negative intracellular diplococci. White blood count was 16,800, while other laboratory findings were negative. She again signed a release after a one-day stay in the hospital.

On her admission to the hospital in February, 1939, the patient complained of a chronic, foul-smelling, vaginal discharge present since shortly after the delivery of her youngest child one and one-half years before. She also complained of pain in the right lower abdomen for about one year. For five months she had suffered from a menorrhagia which had resolved itself into daily bleeding with a severe vaginal discharge two months later, requiring the use of two to three pads daily. She had lost approximately 20 pounds in the six months before this admission.

The positive findings on physical examination were mild tenderness on deep palpation in the right lower quadrant and some pelvic findings which revealed the uterus to be in third degree retrodisplacement. The size was not definitely determined but seemed larger and softer than normal. There was a large cystic, somewhat tender mass about 9 cm. in diameter in the right adnexa. The left adnexa were negative.

A diagnosis was made of (1) right cystic ovary, (2) third degree retrodisplacement of uterus, and (3) severe erosion of the cervix. Laboratory findings were negative.

A total hysterectomy and right salpingo-oophorectomy was performed under ether anesthesia by one of the authors. If tuberculosis of the cervix had been suspected, a more suitable anesthetic would have been used and a bilateral salpingo-oophorectomy performed.

The entire pelvis was filled with fine adhesions. The left tube and ovary were adherent to the posterior wall of the uterus, the right ovary being obliterated by a unilocular cyst measuring 10.5 cm. by 5 cm. in diameter. The sac was thin and filled with a gelatinous material.

Microscopic examination of the cervix revealed partial destruction of the surface epithelium, exposing the underlying cervical glands which were in some instances cystic in character. The stroma showed a marked inflammatory reaction, chronic in character, and in one area near the surface, tubercle-like structures with the characteristic cellular reaction of tuberculosis could be observed without caseous necrosis.

Sections through the endometrium, tubes, and ovaries showed no tuberculosis.

The patient was discharged in good condition on the tenth day after surgery. She was recalled to the hospital eight months later for re-examination. At this time she had no complaints and had gained three pounds in the past month. Pelvic findings were negative. Cystoscopic examination was negative, as was also a retrograde pyelogram. No tubercle bacilli could be demonstrated in either the gastric contents or the urine. The sedimentation rate was rapid; 29 mm. in one hour and 62 mm. in two hours. The chest x-ray picture was negative.

The case of tuberculosis of the cervix presented here appears to be, from the evidence so far at hand, one of the rare instances of primary tuberculosis. No tuberculosis could be demonstrated elsewhere in this patient although a careful search was made for a focus of infection. We feel hesitant, however, about presenting this as a primary case without reservation, since there are several unexplained signs and symptoms which point to a possible focus of tuberculosis elsewhere in this patient.

1. Unexplained hemoptysis in November, 1937.
2. Twenty-pound weight loss in the six months prior to surgery which may have been due to the excessive vaginal bleeding.
3. The pelvic adhesions which may have been on a basis other than tuberculosis. Careful examination failed to reveal involvement of the tube, uterus, or ovary.
4. Increased sedimentation rate in October, 1939, eight months following surgery.

COMMENT

Marked differences of opinion exist as to the method of treatment of genital tuberculosis. Surgery is advocated by a majority of gynecologists, the treatment centering itself around two groups: Those advocating conservative surgical measures, and others who insist that more radical treatment is the method of choice, including subtotal hysterectomy and bilateral salpingectomy, but sparing the ovaries wherever possible. Jameson[13] reports the mortality rate to be 10 per cent higher when conservative operations are performed, and states that the prognosis of untreated or only medically treated cases is grave. He feels further that, although those surgeons endeavoring to remove only diseased structures from the pelvis are following sound gynecologic procedure, they err in that it is impossible to determine the amount of tuberculous involvement of the various structures macroscopically. When the tubes are involved, the surgeon has no alternative but to perform a bilateral salpingectomy, since bilateral involvement is estimated in as high as 90 per cent of the cases.[14] Some authorities insist that tuberculous involvement of the salpinges is always bilateral. Attempts to spare the uterus in these cases is also considered hazardous, since uterine tuberculosis is estimated to exist in well over 50 per cent of the cases revealing tuberculous salpingitis. One or both ovaries may be spared if they do not appear involved, but this should be done with great caution since involvement cannot be ascertained without the aid of the microscope.

King[3] is convinced that surgery should not be performed in the face of an active pulmonary tuberculosis, since the pelvic involvement is not as serious, and surgery may tend only to aggravate the chest condition. He feels that the essential part of the treatment then becomes heliotherapy in a sanatorium and states that this cannot be overemphasized.

X-ray therapy, introduced by Bircher in 1908, has warm advocates[15] and has been used by some with much more success than surgery. The x-ray advocates claim that there is no contraindication to its use and feel that while many will be greatly benefited from surgery, there is an initial operative mortality rate of 7 to 8 per cent, together with a very high incidence of post-operative complications.

SUMMARY

1. This report is based on a study of 15 patients with proved pelvic tuberculosis, operated upon and treated at the Milwaukee County General Hospital in the past eleven years.

2. Significant facts brought out by this study are: (a) Generally all patients afflicted with genital tuberculosis fall into the "childbearing age" group with 80 per cent ranging between 20 and 30 years of age. (b) Pulmonary involvement was encountered in only 20 per cent of our cases. (c) Postoperative complications were high with an average postoperative hospital stay of 43.4 days. (d) Uterine tuberculosis was not encountered in any of our cases.

3. Differential diagnosis remains a major problem with 100 per cent incorrect preoperative diagnosis in our cases.

4. A case of cervical tuberculosis (probably primary) is presented.

REFERENCES

(1) *Stevenson, Charles Summers:* Am. J. Obst. & Gynec. **36:** 1017, 1938. (2) *Finlaison, F. H.:* J. Obst. & Gynaec. Brit. Emp. **43:** 473, 1936. (3) *King, James E.:* Am. J. Obst. & Gynec. **35:** 520, 1938. (4) *Glass, Morris, and Cresci, Joseph:* Am. J. Surg. **41:** 216, 1938. (5) *Stevenson, Charles Summers, and Wharton, Laurence R.:* Am. J. Obst. & Gynec. **37:** 303, 1939. (6) *Bishop, Everett L.:* Am. J. Obst. & Gynec. **19:** 822, 1930. (7) *Danforth, William C.:* Ann. Surg. **106:** 407, 1937. (8) *Schmitz, Herbert E., and Geiger, Clyde J.:* Illinois M. J. **75:** 80, 1939. (9) *Fischer, Henry S., and Held, David:* Am. J. Obst. & Gynec. **37:** 339, 1939. (10) *Collins, Donald C.:* J. A. M. A. **112:** 605, 1939. (11) *Lester, Charles W.:* Am. J. Surg. **33:** 574, 1936. (12) *Douglass, Marion, and Redlon, Magnus:* Surg. Gynec. Obst. **48:** 408, 1929. (13) *Jameson, Edwin M.:* Am. J. Obst. & Gynec. **27:** 173, 1934. (14) *Siddall, R. S.:* J. Michigan M. Soc. **35:** 561, 1936. (15) *Lenz, Maurice, and Corscaden, James A.:* Am. J. Surg. **33:** 518, 1936.

A CLINICAL STUDY OF THE EFFECTS OF DIETHYLSTILBESTROL ON PUERPERAL WOMEN

H. F. Connally, Jr., M.D., D. I. Dann, M.D., J. M. Reese, M.D., and L. H. Douglass, M.D., Baltimore, Md.

(From the Obstetrical Service of the Baltimore City Hospitals)

SINCE the reports by Dodds,[1, 2] in 1938, diethylstilbestrol has been used experimentally by numerous workers and various results have been obtained and reported. Most of the literature deals with the estrogenic activity of this drug in relation to menopausal symptoms and cases of primary and secondary amenorrhea. To our knowledge stilbestrol has been administered to only a few post-partum patients and the reports made with reference to tolerance and the effect of this synthetic estrogen on lactation.[3-5]

Our experiment began with the idea of determining what effects, if any, diethylstilbestrol would exhibit on the puerperal uterus, since urinary estrogen levels are normally low following the third stage of labor;[6, 10] also to determine any alteration in the process of endometrial regeneration. In addition, we became interested in noting whether or not such changes would affect the incidence of puerperal endometritis.

In 1931 Williams, J. W.,[7] studied a large number of puerperal uteri and was able to show "that from about the fourteenth day onward, the uterine cavity outside of the placental site is completely lined by epithelium although several more days elapse before the endometrium can be regarded as fully restored." He also stated that six to seven weeks appeared to be required for the disappearance of the placental site.

Since stilbestrol is two to three times as active as estrone[1] and seems to be equally as effective whether given by mouth or by injection,[1] it occurred to us that this drug might have a stimulating effect on endometrial regeneration. Theorizing further, it was felt that it might maintain a good uterine blood supply,[11, 12] lend a better tone to the musculature by increasing the contractability,[8, 9] sensitize the myometrium to oxytocics,[8] and in this way bring about a greater resistance to puerperal infection and hasten involution.

After a preliminary trial with stilbestrol for three weeks, we found that 5 mg. doses could be tolerated with no apparent side effects; therefore, it was decided to administer the drug in this dosage to 200 consecutive operative obstetric cases, for it is in this group that the highest incidence of morbidity occurs. Our series began Jan. 19, 1940, and ended April 30, 1940, covering a period of the year in which our morbidity level is usually at its peak.

MATERIAL

Each operative case, excluding cesarean section, received 5 mg. of stilbestrol in oil intramuscularly within the first six to twelve hours following delivery and then received 5 mg. by mouth each morning until the day of discharge which was usually the tenth post-partum day. The average amount of stilbestrol received by each patient was 50 mg. This routine was carried out on 105 patients, after which time our supply of stilbestrol was exhausted. Ten days later the second series of cases was begun and for this group the dosage was changed. Each patient received 10 mg. of stilbestrol each day for the first three days and then 5 mg. a day for the remaining time in the hospital. During the first three days, one-half of the dose was given intramuscularly in oil. This procedure was carried out on 95 patients, making a total of 200 cases studied.

Thirty patients delivering spontaneously received diethylstilbestrol in 5 mg. doses daily, and in 23 of these attempts at endometrial biopsy were made, only one specimen being obtained from each patient. The time of biopsy varied from the eighth to the fourteenth post-partum day. The tissue for microscopic examination was removed with a biopsy forceps and curette. Because of the care which had to be used in such procedures, the specimens obtained were unsatisfactory in that they contained a large amount of cervical glands, endometrial stroma, and debris. None of the specimens showed amounts of endometrium sufficient to allow definite conclusions to be drawn. It was felt that further attempts at biopsy should be discontinued because of the added risk of infection and perforation of the uterus to the patient.

In the group of 200 cases studied, the following operative procedures were carried out at the time of delivery:

Episiotomy	194
Low forceps	189
Mid forceps	4
Breech extraction	5
Occiput posterior rotated with forceps	6
Occiput posterior rotated manually	2
Occiput transverse rotated with forceps	9
Occiput transverse rotated manually	6
Manual removal of placenta	2

Caudal block anesthesia was used in 178 of the 200 patients delivered. Gas-oxygen or gas-oxygen-ether was used in the remainder.

Our usual post-partum technique was carried out on all patients. Following delivery of the placenta, each patient received one ampoule of pitocin (½ c.c.) and if bleeding was excessive, ergonovine, ampoule 1, was given intravenously.

Routinely, each patient received 0.2 mg. of ergonovine by mouth every four hours for 6 doses. This was repeated in the majority of cases on the third post-partum day.

RESULTS

Toxic Effects of the Drug.—Of the 200 patients receiving stilbestrol, not a single side effect was noted that could be attributed to the drug. One patient developed a generalized urticarial rash on the seventh post-partum day, but this was most probably due to a barbiturate she received the night before, since she gave a history of previous attacks.

As already noted by Greenhill,[3] puerperal women apparently have a "special tolerance to the drug." The fact that they were kept in bed may have influenced somewhat the toxic effects. However, if the toxic action of stilbestrol is central, we should have witnessed a higher incidence of toxic symptoms.

Sensitization of the Uterus to Oxytocics.—For the first four days post partum, it was observed that the uterus responded better than usual to oxytocics. This was purely a clinical observation and was not supported by experimental data.

Lactation.—Lactation was suppressed in 70.5 per cent, or 141, of the 200 cases reported here. With the dosage used we did not succeed in completely inhibiting lactation in a single incidence, although its onset was delayed to about the fifth or sixth day. It was interesting to note that none of the patients complained of engorged or otherwise painful breasts.

Lochia.—The flow of lochia did not seem to be changed in any way except that there was an increased flow in the seven cases of puerperal endometritis.

Post-partum Examination at Time of Discharge.—The vaginal mucosa was conspicuously pale and appeared to have shrunk somewhat as contrasted to the congested friable mucosa of the untreated cases. The cervix except for its mucosal surface showed no changes grossly. Of the 200 patients examined, 172, or 86 per cent, showed normally involuting uteri. Twenty-eight, or 14 per cent, of the patients showed enlargement of the uterus and were classified as subinvoluted. Five of these patients returned within two weeks after discharge and showed well involuted uteri. No treatment had been advocated or followed in these cases.

Effects Observed Clinically on Morbidity.—The total number of patients having a temperature elevation to 100.4° F. or more at any time during the puerperium, excluding the first twenty-four hours immediately post-delivery, was 26, or 13 per cent, of the cases. The total number showing a single elevation to 100.4° F. or more was 16, or 8 per cent, of the cases. There were two cases or 1 per cent of the total that had two or more elevations to 100.4° F. or higher within a single twenty-four-hour period not classified as morbid.

For our morbidity standard, the first twenty-four hours post partum were excluded. After that, any patient who had two or more elevations to 100.4° F. or above on any two twenty-four-hour periods was classified as morbid. Temperatures were recorded every four hours.

On the basis of the above standard, 8 cases or 4 per cent of the 200 cases studied were morbid. One of these patients had pyelitis and 7 had puerperal endometritis. The corrected morbidity rate was 3.5 per cent. These figures are considerably lower than any obtained in this clinic previously. The total morbidity for 193 patients delivered by operative procedures between Oct. 1, 1939 and Dec. 31, 1939, receiving only the routine post-partum care, was 16.6 per cent. The total morbidity of the clinic during the same period last year, Jan. 1, 1939 to April 1, 1939, was 13.65 per cent, including all cases.

The results we obtained in our series affected the total morbidity of the clinic as follows: Total morbidity from Jan. 1, 1940 to April 1, 1940, 9.7 per cent. Operative morbidity during the same period, including 196 low forceps, 5 mid-forceps, and 21 breech extractions, 10.04 per cent.

To date, 20 per cent of the patients treated have been examined on or about the twenty-first post-partum day. In all cases the uterus was well involuted and approaching normal size. Lactation seemed to return in those patients who continued nursing their babies after the stilbestrol was discontinued. There were no complaints concerning the breasts. All patients reported a slight bloody discharge for one day to two weeks after leaving the hospital. This does not seem to vary from the usual post-partum course.

SUMMARY

Diethylstilbestrol was administered to 200 puerperal women in an attempt to show the effects of estrogens on the post-partum uterus with special reference to endometrial regeneration. Due to unforeseen difficulties, our primary objective could not be reached, but certain interesting clinical observations were noted and considered worthwhile reporting.

CONCLUSIONS

1. In this group of women no case under observation showed any single toxic side effect, even though the drug was pushed to more than the usual therapeutic dose.

2. From clinical observation only, these uteri sensitized by the drug apparently responded more readily to oxytocics than those in the control group.

3. Lactation was apparently suppressed in 70.5 per cent of the cases observed. However, in the dosage used complete inhibition was not noted, although the onset of lactation was delayed longer than in the control group. No incidence of engorged or painful breasts was noted in the treated group.

4. Clinically, the flow of lochia was not materially changed.

5. Stilbestrol apparently had no immediate effect on early involution of the puerperal uterus; however, pelvic examinations on about the twenty-first post-partum day revealed a more rapid involution than occurred in the control group.

6. Whatever the effects of stilbestrol on the parturient uterus may be, it was noted from the clinical standpoint that our morbidity in treated patients was materially affected, being 4 per cent as against a total morbidity of 12.8 per cent for the year 1939. Since our series included only operative cases, it would be supposed that the morbidity rate would be higher than the 12.8 per cent figure for 1939, which included normal as well as operative deliveries.

7. At this time we cannot advocate the routine use of diethylstilbestrol in the prophylactic therapy of puerperal endometritis; however, we hope that further investigations on this subject will be carried out.

Biopsy specimens were prepared and examined by the University of Maryland Department of Pathology.

The diethylstilbestrol used in this experiment was supplied by Abbott Laboratories.

REFERENCES

(1) *Dodds, E. C., Goldberg, L., Lawson, W., and Robinson, R.:* Nature **141:** 247, 1938. (2) *Dodds, E. C., Lawson, W., and Noble, R. L.:* Lancet **1:** 1389, 1938. (3) *DeLee, J. B., and Greenhill, J. P.:* Year Book of Obstetrics and Gynecology, p. 604, Ed. note, 1939. (4) *Winterton, W. R., and MacGregor, T. N.:* Brit. M. J. **1:** 10, 1939. (5) *Kellar, R. J., and Sutherland, J. K.:* J. Obst. & Gynaec. Brit. Emp. **46:** 1, 1939. (6) *Wolf, William:* Endocrinology in Modern Practice 1936, p. 580. (7) *Williams, John Whitridge:* AM. J. OBST. & GYNEC. **22:** 664, 1931. (8) *Wolf, William:* Endocrinology in Modern Practice, 1936, p. 577. (9) *Falls, F. H., Lackner, J. E., and Krohn, L.:* J. A. M. A. **106:** 271, 1936. *(10) *Zondek, B.:* Die Hormone des Ovariums und des Hypophysenvorderlappens, Berlin, 1931, Julius Springer. (11) *Markee, J. E.:* Am. J. Physiol. **100:** 32, 1932. *(12) *Pompen, A. W. M.:* De Invloed van Menformon op de Baarmoeder, Thesis, Amsterdam, 1933.

*Obtained from *Reynolds, S.R.M.:* Physiology of the Uterus, 1939.

NORMAL VARIATIONS OF FETAL HEART RATE DURING PREGNANCY

LESTER WARREN SONTAG, M.D., AND HELEN NEWBERY, M.A.,
YELLOW SPRINGS, OHIO
(From the Samuel S. Fels Research Institute, Antioch College)

OF THE limited number of criteria which are available for judging the state of well-being of the fetus during pregnancy and labor, the rate and variations of rate of the fetal heart are usually considered among the most important. There are two reasons for the stress laid upon fetal heart rate as an indicator of the condition of the fetus. Perhaps the first reason is that it is one of the few physiologic phenomena of the fetus which may be observed accurately and at will. Second is the fact that fetal distress in the form of anoxemia is widely believed to manifest itself earliest through a change in cardiac rate. We do not mean to imply that asphyxia is considered the only cause of abnormal deviation in heart rate. Leff[1] has advanced the theory that marked slowing of the fetal heart is the result of an overdistention of the fetal circulation from squeezing out of the blood from the placenta in prolonged labor.

There is not clear agreement as to what constitutes an abnormal heart rate.

The figure frequently found in American textbooks (Curtis,[2] Williams,[3] etc.) is above 160 or below 100. Many authors consider that heart rates above or below these figures imply fetal distress and are usually an indication for operative interference. Bartholomew[4] states that, while a rate of 160 or above is considered dangerous, he does not find it so. He believes, on the other hand, that a rate below 120 is a signal of distress, indicating asphyxia. Richardson[5] considers that a fetal heart rate of 150 to 160 in ablatio placentae indicates one-fourth separation of the placenta and from 170 to 190, one-half separation of the placenta. Sachs[6] fixes the normal range of fetal heart rate at from 132 to 144. He considers that figures below 100 and above 160 are not without physiologic "consequences." While he states that rates above 160 are abnormal they are not in themselves indication for forceps delivery. He believes that wide fluctuation indicates danger. Willibald[7] believes that slow fetal heart rates during labor are more commonly due to pressure exerted on the head than to interference with fetal maternal gaseous interchange. Rech[8] says that the fetal heart rate is not changed either by oxygen deficit or excess carbon dioxide in the fetal blood. Bartram[9] concluded that it was impossible to determine the exact causes of changes in fetal heart rate during labor. In some of his cases, slowing of heart rate to 100 or below for an hour was harmless. In other cases, irregularities for a much shorter time were followed by death.

At the Samuel S. Fels Research Institute we have had under observation during the last half of pregnancy some 200 women. Of these, 63 have been available for repeated observations on fetal heart rate. We have, therefore, been able to accumulate from these 63 women a large amount of data on fetal heart rate during the sixth, seventh,

eighth, ninth, and tenth lunar months. Mothers are available for observations either once each day or once each week, and the fetal heart is recorded at each of these instances over one or more five-minute periods. We have accumulated, therefore, many thousands of minutes of heart records. The methods of recording have been described elsewhere.[10] From this material we have selected all records taken under conditions of no known stimulation to either mother or fetus, to determine the frequency with which rates of 160 and above, and 120 and below, are to be found during these normal pregnancies before labor had begun. We have available 18,517 half-minute samples of such "normal" fetal heart rate. Eighty per cent of these were collected during the ninth and tenth months of pregnancy. To us it seems very doubtful whether fetal heart rates which occur normally during the ninth and tenth lunar months can be considered evidences of fetal distress during labor.

Table I shows the number of fetuses whose heart rate was 160 or above during one or more of the sampling periods. It also shows the total number and percentage of half-minute rates which were above this figure. The distribution of rapid rates varies tremendously. Rapid rates are sometimes maintained for a number of consecutive half-minute periods. In other instances the rate rises from 130 or 140 beats per minute to 170 or more and returns within a minute. Wide and rapid fluctuations without apparent cause other than bodily activity are common. Table II shows the same type of data for rates which dropped below 120. As indicated by the table, rates below 120 before labor are rare.

TABLE I. NUMBER AND PERCENTAGE OF FETUSES AND HEART RATE SAMPLES SHOWING RATES OF 160 AND ABOVE

MONTHS	TOTAL CASES	CASES WITH RATES 1 OR MORE TIMES ABOVE 160	%	TOTAL ½ MINUTE SAMPLES OF HEART RATE	NO. OF SAMPLES ABOVE 160	%
10	50	39	78	8963	539	6.2
9	46	33	72	5303	441	8.3
8	41	21	51	2787	136	4.9
7	22	10	45	991	91	9.1
6	10	7	70	484	84	17.3

TABLE II. NUMBER AND PERCENTAGE OF FETUSES AND HEART RATE SAMPLES SHOWING RATES BELOW 120

MONTHS	TOTAL CASES	CASES WITH RATES 1 OR MORE TIMES BELOW 120	%	TOTAL ½ MINUTE SAMPLES OF HEART RATE	NO. OF SAMPLES BELOW 120	%
10	50	14	28	8963	39	0.4
9	46	8	17	5303	23	0.4
8	41	4	10	2787	11	0.4
7	22	1	4	991	1	0.1
6	10	0	0	484	0	0

Fig. 1 shows the incidence of half-minute heart rates which exceed 160 beats per minute for all cases and all months of pregnancy. It gives no indication of the degree to which the 160 beat rate was exceeded, but shows the frequency with which excessive rates occurred in the group. This histogram indicates that for 81.2 per cent of the group some samples exceeding 160 would be expected in

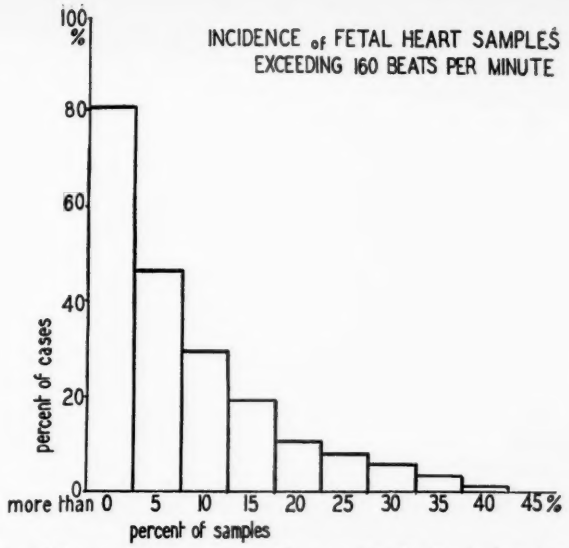


Fig. 1.—This histogram shows the incidence of half-minute heart rate samples in our 63 cases which exceeded 160 beats per minute any time during the last five lunar months of pregnancy.

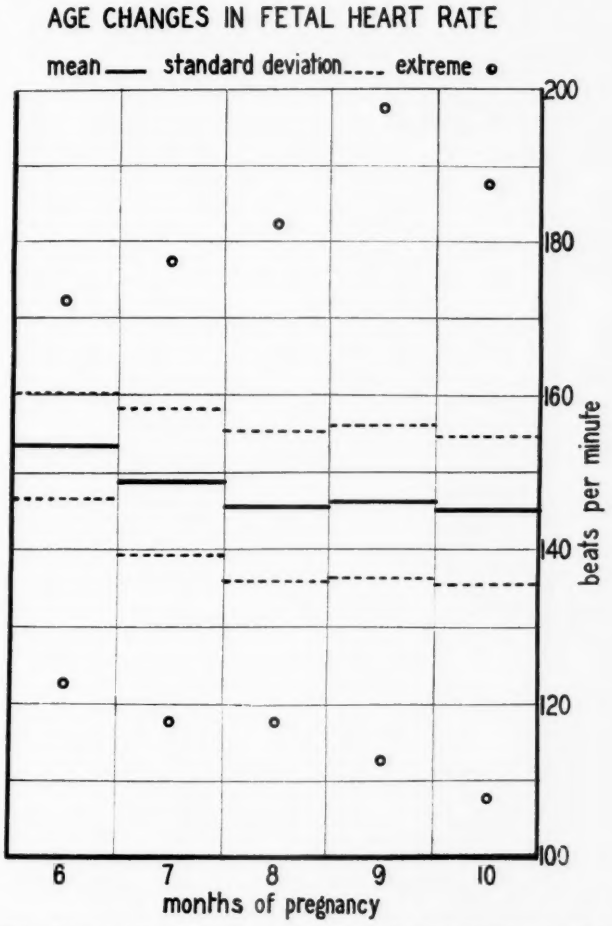


Fig. 2.—This diagram presents the means, standard deviations, and extremes for the total number of heart rate samples for each month of pregnancy. The extremes ranged from 105 to 200 beats per minute.

every 100 samples studied. For 46.9 per cent of the group five or more extreme samples would be expected in every 100, for 29.7 per cent of the group, 10 or more in every 100, and so on. Fig. 2 presents means, standard deviations and extremes for the total number of heart rate samples studied in each month of pregnancy. The extremes of our "normal" samples ranged all the way from 105 to 200 beats per minute. We found no instances where the rate dropped below 100 for a period of one-half minute or more. Short periods of very slow rate, lasting only a few seconds, occur not infrequently. They are of too short duration, however, to be apparent in a half-minute sample.

It should be emphasized here that all of these fetal heart rates were taken before the onset of labor. In those instances in which the rate has arisen above 160 or dropped below 120, there can be no question, therefore, of obstetric emergency, nor is there any reason to suspect anything abnormal about the selection of the cases. Mothers who volunteered for this study did so as a part of their participation in the general program of the Fels Research Institute and in no instance because of illness or suspicion of fetal abnormality. Heart rates which in this group have been found to be beyond what are commonly defined as normal limits have been beyond these limits without the existence of pathologic labor factors.

SUMMARY

The analysis of 18,517 half-minute samples of fetal heart rate on 63 normal fetuses ranging throughout the last five lunar months of pregnancy shows that rates of 160 or more beats per minute are common. Rates below 120 beats per minute are, on the other hand, unusual. Rates below 100 were not found in our group. Marked fluctuation in rate is frequently found.

CONCLUSIONS

Increase in fetal heart rate above 160 per minute occurs so frequently during the two months preceding labor that occurrence during labor seems little justification for assuming fetal distress. Marked fluctuations in rate are common during the last two months of pregnancy in normal fetuses. Since rates below 100 were not found in our group, it seems justifiable to conclude that low rates are as a rule the direct result of the effects of labor. High rates occur normally during the latter months of pregnancy and should be interpreted with caution when found during labor.

REFERENCES

(1) *Leff, M.:* Am. J. Obst. & Gynec. **24:** 898, 1932. (2) *Curtis, A. H.:* Obstetrics and Gynecology, Vol. II, Philadelphia, 1933, W. B. Saunders Co., p. 80. (3) *Williams, J. W.:* Obstetrics, New York, London, 1924, D. Appleton & Co., p. 207. (4) *Bartholomew, R. A.:* Am. J. Obst. & Gynec. **10:** 89, 1925. (5) *Richardson, G. C.:* Ibid. **32:** 429, 1936. (6) *Sachs, E.:* Ztschr. f. Geburtsh. u. Gynäk. **82:** 284, 1920; Abst. J. A. M. A. **76:** 417, 1921. (7) *Willibald, W.:* Ztschr. f. Geburtsh. u. Gynäk. **101:** 724, 1932. (8) *Rech, W.:* Arch. f. Gynäk. **147:** 82, 1931. (9) *Bartram, G.:* Ztschr. f. Geburtsh. u. Gynäk. **84:** 33, 1921; Abst. J. A. M. A. **78:** 554, 1922. (10) *Sontag, L. W., and Richards, T. W.:* Child Development Monographs **3:** 7, 1938.

INTRAUTERINE ONSET OF HEMORRHAGIC DISEASE OF THE NEWBORN

CARL T. JAVERT, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, New York Hospital and Cornell University Medical College)

HEMORRHAGIC disease of the newborn is generally believed to have its onset from the second to the sixth day of life, as shown by the reports of Diamond, Salomonsen, and others. In a recent paper,[4] I stated that the clinical evidence of bleeding occurred on the first day in over one-third of my cases. This observation stimulated the conclusion that the disease runs part of its course in utero, and that antenatal and intranatal factors are contributory. I called attention to the higher incidence of antepartum complications of pregnancy, namely, anemia, toxemia, and treated syphilis, in the mothers of these infants. It was observed further that labor was often prolonged, or if short, that the uterine contractions were unusually strong. Each contraction of the uterus expresses blood from the placenta into both the arterial and venous portions of the fetal circulation; the patent ductus venosus, ductus arteriosus, and foramen ovale permit the increased pressure to be distributed to all parts of the body of the infant. This results in separation of the endothelial cells of the capillaries and probably explains the development of petechiae and ecchymoses in the internal organs and soft tissues in a varying degree. This may occur even after a normal labor. These hemorrhages may be regarded as physiologic and probably become pathologic when the coagulation mechanism is deranged. On the basis of this evidence I concluded that "abnormal clotting factors do not produce hemorrhages per se, but rather allow bleeding precipitated by the forces of labor to continue."

The development of bleeding from the fetus while still in utero was observed recently in three cases of hemorrhagic disease, two of which were associated with bloody amniotic fluid, and in the third case, intraplacental and retroplacental hematomas were observed. In each instance labor was short but severe, with long hard uterine contractions.

CASE 1.—This negro mother was a 37-year-old primigravida, with a 4-plus Wassermann discovered during pregnancy, for which she was given 3.3 Gm. of neoarsphenamine and 0.2 Gm. of bismuth during the antenatal course. A moderately severe pre-eclamptic toxemia developed, with rise in blood pressure to 165/110 mm. albuminuria, and a uric acid content of 10.8 mg. per 100 c.c. The patient did not respond to the usual measures, including intravenous glucose, and developed epigastric distress with nausea and vomiting. The weight during pregnancy had not increased appreciably. In the thirty-eighth week of gestation a medical induction of labor was done, with castor oil, quinine and nasal pituitrin, because of the toxemia. It was successful. The contractions became so severe that the nasal pituitrin was discontinued after the second dose. Ultimately open drop ether was necessary during contractions in order to secure proper relaxation of the uterus, although at no time was the fetal heart irregular. The membranes presented at the introitus when the cervix was 8 cm. dilated, and were ruptured artificially

under direct vision, and blood-tinged amniotic fluid escaped. No analgesia was given other than the open drop ether, and after a strong labor of six and one-half hours, a spontaneous delivery occurred (March 17, 1938). The infant (male) weighed 3,070 Gm., did not require resuscitation, and appeared to be in good condition.

Three hours after birth bright bleeding was observed from the penis and mouth of the child and a bloody dejection took place. Petechiae were seen in the skin of the buttocks. The red cell count was 3,500,000, white cell count 41,500, and two nucleated red cells were counted per 100 white cells. The bleeding time was 60 minutes, and the clotting time was 10 minutes. The child was cyanotic at times. A transfusion of 60 c.c. of blood was given. The child died four hours later, or thirteen hours after birth. A blood culture was negative after five days of incubation, and the Wassermann reaction was 4-plus. Autopsy was permitted, and the positive findings included slight subarachnoid hemorrhage, petechiae and hemorrhages into the lungs, thymus, epicardium, myocardium, and scalp. No evidence of syphilis was found in the liver, and the epiphyseal line of the femur was normal. The placenta weighed 530 Gm., and careful inspection of the membranes and fetal surface failed to reveal vascular lesions that might produce the bloody amniotic fluid. On histologic section no evidence of syphilis was apparent. The death was attributed to hemorrhagic disease of the newborn.

CASE 2.—The mother, a 28-year-old, para 5-0-0-4, negro, had a 1-plus Wassermann reaction. She had stigmas of congenital syphilis, including eighth nerve deafness and Hutchinsonian teeth. She was given 2.25 Gm. of neoarsphenamine, 1.1 Gm. of arsphenamine, and 0.6 Gm. of bismuth during the antenatal course. A secondary anemia developed (the hemoglobin was 58 per cent, with a packed cell volume of 28 per cent), which responded to treatment. In addition a Type V pneumococcus lobar pneumonia developed in the seventh month of gestation for which 440,000 units of horse serum were administered. The weight remained stationary after the pneumonia, and there was no sign of toxemia of pregnancy. Labor occurred spontaneously in the forty-first week of gestation and continued without analgesia. The delivery (Feb. 13, 1939) was also spontaneous, after a hard type of labor with a total duration of only three hours and twenty-three minutes of which only eight minutes was spent in the second stage. At this time the membranes were observed to rupture with a gush of blood-stained fluid, more of which was noted immediately after the birth of the baby. The placenta weighed 750 Gm., and careful examination of the fetal surface and of the membranes failed to disclose any source for the blood in the amniotic fluid. Histologic section failed to reveal any evidence of syphilis.

The infant (female) weighed 3,780 Gm., and required simple resuscitation. Bleeding began three hours after birth, and was observed from the mouth and also as a copious bloody stool. The red cell count was 4,200,000, hemoglobin 69 per cent (16 Gm.), white cell count was 26,100, with 17 normoblasts per 100 white cells in the smear. The bleeding time was two and one-half minutes, and the clotting time was nine minutes. Three transfusions were given (total 155 c.c.) with cessation of the bleeding. The neonatal course was complicated by a mild gastrointestinal upset, but the infant was ultimately discharged as well. The Kline and Wassermann reactions were both negative on the infant's blood.

CASE 3.—The mother was a 22-year-old white primigravida, with a negative Wassermann reaction. Her antepartum course was complicated by slight vaginal bleeding in the twenty-seventh week of gestation. Examination at that time revealed a uterus of normal development, relaxed, and the cervix was tightly closed and presented a large erosion which bled easily, to which the bleeding was attributed. There was no evidence of toxemia. The pregnancy continued without further bleeding until the thirty-sixth week of gestation when labor began spontaneously. The patient was admitted to the hospital having very strong contractions lasting up to two minutes, the uterus relaxed poorly, and the cervix was almost fully dilated. A considerable bloody show was evident but was considered no more than ordinary. The patient delivered (May 14, 1939) soon after admission and after a total labor of five hours, no analgesia having been given. The meas-

ured blood loss in the third stage was 200 c.c. The placenta weighed 515 Gm. The maternal surface had six definite hematomas of varying depth and size, the largest measuring 5 by 2 by 2 cm. The margins of these showed definite organization and contained old tarry blood, and in others more recent clotted blood. On histologic section very definite hematomas were recognized.

The infant (male) weighed 1,980 Gm., and required resuscitation with carbon-dioxide-oxygen mixture. He had repeated cyanotic spells and soon began to bleed from the cord, nose, and mouth, and there was evidence of slight left facial paralysis. Death occurred four hours after birth, and just before transfusion was to be given. The Kline reaction was negative, the blood culture was negative, and spinal puncture yielded a slightly zanthrochromatic fluid which contained a few red cells. An autopsy was not permitted. Clinically, the cause of death was attributed to hemorrhagic disease and intracranial hemorrhage. Blood was taken at the time of delivery from the mother and from the cord blood of the placenta for prothrombin determinations. The mother had a packed cell volume of 31 per cent, and her prothrombin concentration was 83 per cent of normal; the infant had a packed cell volume of 49 per cent, and had a prothrombin level of 13 per cent of the adult normal. (Titration method of Warner, Brinkhous, and Smith was used.)*

DISCUSSION AND SUMMARY

In the 3 cases of hemorrhagic disease presented, clinical evidence of bleeding was apparent several hours after birth (first day of life). In each instance labor was severe and of short duration. The development of bleeding from the fetus while still in utero was evidenced by bloody amniotic fluid when the membranes ruptured in 2 cases, and by old and recent retroplacental hematomas in the third case. In the latter case the view is taken that these hemorrhages were probably of fetal rather than maternal origin, since the placenta is a fetal organ. These findings support the original observations of the author regarding the intrauterine course of hemorrhagic disease and suggest that the bleeding is probably precipitated by the forces of labor. Such physiologic bleeding becomes pathologic and continues because of a deranged clotting mechanism. This point receives further substantiation by a review of over 700 infants delivered by cesarean section in this Clinic; only one child so delivered had the disease, and it had experienced a labor of sixty hours before delivery. However, the case reported recently by Brinkhous, Smith and Warner had been delivered by cesarean section, which at first seems to discount this finding, but their patient also had a severe toxemia for which reason the cesarean section was performed.

The prothrombin concentration in the newborn infant has been studied by many investigators including Quick and Grossman, Brinkhous, Smith and Warner, Shettles, Delfs and Hellman, Kugelmass, Waddell and Guerry. Javert and Moore have had the opportunity of recording blood plasma prothrombin determinations in 20 parturient women at term and in the cord blood of their infants. The average concentration was 23 per cent, using the method of Warner, Brinkhous, and Smith, which is in agreement with 26 per cent obtained by Brinkhous, Smith and Warner. The low concentration of 13 per cent or half of the normal newborn level in Case 3 seems doubly significant since the child developed retroplacental hemorrhages as well as hemorrhagic

*These determinations were made possible through the courtesy of Dr. William DeWitt Andrus under a grant from the John and Mary R. Markle Foundation.

disease. It seems plausible to consider the hematomas in the placenta as of fetal origin probably developing on the basis of low prothrombin concentration in the infant. While no prothrombin determinations were done on Cases 1 and 2, it may be possible that they were also very low, since the mothers of both infants had received antisyphilitic therapy which may have had an effect on prothrombin formation in these infants.

The recent work of Shettles and Hellman on the administration of synthetic vitamin K to mothers in the last month of pregnancy and during labor showed that the level in the infant could be raised 3 times the usual level. Waddell and Guerry have given it to the infant after delivery and have raised the prothrombin level. The prophylactic use of vitamin K therapy in mothers and their infants with prolonged labors, short severe labors, toxemia of pregnancy, treated syphilis, may lower the incidence of hemorrhagic disease, and (nontraumatic) intracranial hemorrhage.

CONCLUSION

Three cases of hemorrhagic disease which developed the first evidence of bleeding in utero were presented. Two patients had bloody amniotic fluid, and the third patient had intraplacental and retroplacental hematomas, with a prothrombin concentration of only 13 per cent of the adult normal, while the mother's concentration was normal. The low prothrombin concentration in the infants may be the precipitating factor in cases of premature separation of the placenta. The probable role of labor in producing hemorrhages and of a deranged clotting mechanism in permitting these to continue was mentioned. The reduction in prothrombin concentration in infants following maternal antisyphilitic therapy was postulated.

REFERENCES

(1) *Brinkhous, K. M., Smith, H. P., and Warner, E. D.:* Am. J. M. Sc. **193:** 475, 1937. (2) *Diamond, L. K., Blackfan, K. D., and Baty, J. M.:* J. Pediat. **1:** 269, 1932. (3) *Hellman, L. M., and Shettles, L. B.:* Bull. Johns Hopkins Hosp. **65:** 138, 1939. (4) *Javert, C. T.:* Am. J. Obst. & Gynec. **35:** 200, 1938. (5) *Javert, C. T., and Moore, R. A.:* Personal communication. (6) *Kugelmass, I. N.:* Am. J. Obst. & Gynec. **38:** 259, 1934. (7) *Quick, A. J., and Grossman, A. M.:* Proc. Soc. Exper. Biol. Med. **40:** 647, 1939. (8) *Salomonsen, L.:* Acta Paediat. **27:** Supp. I, 1939. (9) *Shettles, L., Delfs, E., and Hellman, L. M.:* Bull. Johns Hopkins Hosp. **65:** 419, 1940. (10) *Waddell, W. W., and Guerry, DuP.:* J. A. M. A. **112:** 2235, 1939. (11) *Warner, E. D., Brinkhous, K. M., and Smith, H. P.:* Am. J. Physiol. **114:** 667, 1935.

THE EFFECT OF CYSTINE ON HUMAN MILK PRODUCTION

R. G. Daggs, Ph.D., Burlington, Vt.

(From the Department of Physiology, College of Medicine, University of Vermont)

THE effect of diet upon milk production has constituted a matter of interest to many investigators.

Ssubotin,[1] in 1886, working with dogs found that the diet had an important effect upon the composition of the milk. Voit,[2] in 1869, showed that a high protein diet was particularly effective in stimulating milk production. Hoobler[3] studied the effect of various forms and quantities of protein upon human milk production. His work brought out the importance of a diet relatively high in good quality animal protein. The findings of Adair,[4] using a large series of human subjects, further emphasized the advisability of a high protein diet. Hitchcock[5] has shown that rats raised larger and healthier litters when they were fed meat in addition to an adequate balanced diet. Daggs,[6] working with dogs, showed liver to be the best source of protein of those tried.

The conclusions were borne out not only by the quantity of milk produced but by the quality as well. The nitrogen retention in the mother was better and the growth of the pups superior for those animals receiving the liver diet.

The next step was to find what factor in the liver was acting as the lactagogue.

Wilkinson and Nelson[7] claimed fresh liver contained a lactation-promoting substance that was destroyed at 120° C. and was not soluble in ether. Smith and Seegers[8] found an alcohol and water soluble, ether insoluble substance in liver capable of stimulating lactation in rats. Mapson[9] demonstrated the presence of a lactagogue which he called "physin" in a water extract of autolyzed liver. Nakahara and his associates,[10] in a series of papers, show evidence for the existence of a lactation vitamin (L_1) that may be obtained from beef liver. Daggs and Tomboulian[11] demonstrated that protein degradation products, extracts and amino acids that contained the lactation principle all had a relatively high sulphur content. Daggs and Lidfeldt[12] showed that cystine, cysteine, and methionine acted as lactagogues. Wright and Haag[13] presented evidence that the lactation-promoting properties of rations containing alfalfa proteins were markedly enhanced by the addition of cystine. In another paper,[14] they postulated the belief that cystine and methionine serve to make sulphur-deficient protein nutritionally complete rather than to act as lactation stimulants per se. It is our belief that the S-H-containing amino acids do more than this. Daggs and Tomboulian[11] pointed out that, "It is definitely known that casein is relatively low in cystine and it may be surmised that the added cystine is merely making a more complete protein of casein. But liver and egg are both considered sources of good complete proteins, and even when fed at practically two times the level they did not give as good results as the casein plus cystine diet." The S-H compounds evidently are utilized in the secretion of milk as Harding and Cary[15] suggested. Whether they act directly upon the mammary gland cells or through the pituitary we cannot say as yet. Recent work concerning the action of glutathione on cellular proliferation would tend to support the former view. The fact that prolactin contains sulphur (White and others[16]) may suggest the idea that cystine is needed by the pituitary to produce prolactin. However, the hormone prolactin does not have the same marked effect upon human beings that it does on pigeons. Ross[17] has shown that it takes very large doses of prolactin to increase milk production even to a slight extent in human beings.

EXPERIMENTAL WORK AND DISCUSSION

Four cases are presented, one of which was studied for over three months. All patients were multiparas having a history of either failing or no milk supply with previous babies. In the first three cases the patients were allowed the regular hospital ration. In addition 1 Gm. each of cystine, glycine and glutamic acid was given with breakfast, 2 Gm. of each of the amino acids with dinner, and 2 Gm. with supper, making a total of 5 Gm. each per day. This combination of amino acids was used in order to allow the body material to manufacture glutathione. The suggestion came from the work of Daggs and Tomboulian.[11] It is not advisable to give too large a dose of cystine for fear of damaging the kidney (Curtis and others[18]). A diet high in the B vitamins, however, protects against this damage to a great extent (Hartwell[19]). None of these cases showed any sign of kidney disturbance even though one of the subjects had a moderate albuminuria before delivery. The amino acids were either sprinkled on the food or given in lemonade. All patients were cooperative and in favor of the experiment. The milk production was obtained by weighing the baby before and after nursing. Nursing was followed by pumping the breasts in the third case. Observations were made until the time of leaving the hospital. No means were available in these three cases for collecting data after that time. The results of the first three cases are shown in Fig. 1.

The patient in Case 1 showed no signs of milk secretion until the eleventh day. Just before leaving the hospital an additional 28 Gm. were obtained by breast pump (shown by the shaded area in the chart).

The patient in Case 2 was seen on the evening of the sixth day post partum, having shown no milk secretion. The amino acid feeding was started at breakfast the next morning. At 2 o'clock that afternoon 50 Gm. of milk were obtained by the infant from the breast. The following day the patient complained of engorged breasts. It might be argued that the milk was slow in starting to be secreted and would have started on the seventh day regardless of the feeding regime. This seems improbable since milk secretion generally begins before this time and the patient had a history of a lack of milk secretion with the previous baby.

Case 3 is particularly interesting since it was obtained sooner, second day post partum. The history revealed the following: Baby born three years before. Put to breast continuously for three months without obtaining any milk. Baby had to be given full formula from the third day on. . . . In this instance both the amount obtained by the baby and that by pump are recorded. It might be said that the application of the breast pump had a great deal to do with the milk flow, but a strong healthy baby was unable to obtain any milk during the previous confinement. Because of the many factors that may have influenced the results of the first three cases and because of the short periods of observation, it was decided that a longer more critical study of the next case should be made.

Case 4 was a multipara free from any metabolic or pathologic disturbance. She had had two children. The first child had been conscientiously put to the breast for a month but obtained very little milk and had to be given full formula at every feeding. The second child, born two years later, also was unable to obtain more than a small amount of colostrum. Three and one-half years later the third child was born. The growth of the baby, the milk production, and the amounts of cystine fed are shown in Fig. 2. Only a small amount of colostrum was obtained by the baby, and formula was given the first few days as indicated on the chart by the letter *F*. On the seventh day, when it seemed apparent that the milk production probably would be slight, 2 Gm. of cystine were given. From then

on to the eightieth day when the milk was taken for analysis, the infant received sufficient milk from the breasts to maintain a normal growth rate. On the twelfth day, two days after leaving the hospital, the patient developed a tetany and engorged breasts which were relieved by using the breast pump. The tetany probably was caused by the sudden shift of calcium from the body tissues to the milk. The milk production continued normal without cystine feeding until the thirty-eighth day when the baby appeared hungry and its weight curve began to flatten. On the thirty-ninth day, cystine again was given as shown on the chart. The patient learned to adjust the cystine dose so as to maintain normally filled

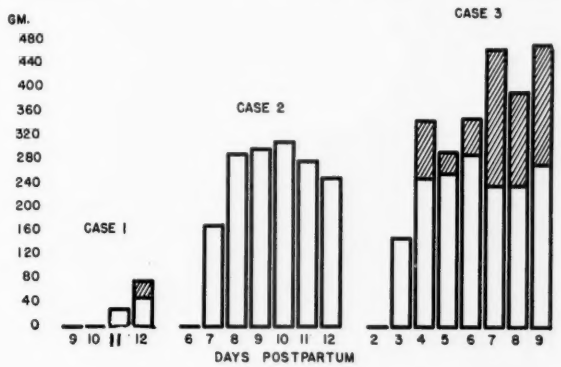


Fig. 1.

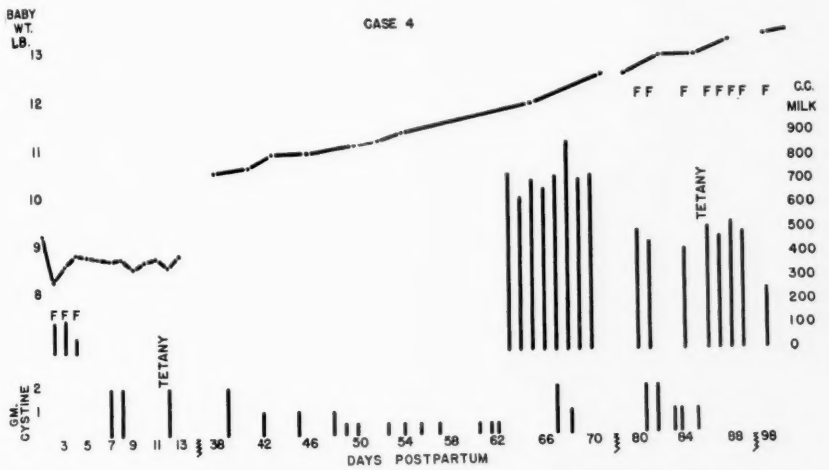


Fig. 2.

breasts. From the sixty-third to the seventieth day, the breasts were pumped, the milk measured, and then given to the baby by bottle. This procedure provided quantitative milk production data as shown in Fig. 2. The infant began taking cereal on the sixty-third day. The baby was put back to the breast from the seventy-first day to the eightieth day when the milk again was obtained by pump and analyzed for fat, carbohydrate, and protein. The results are shown in Table I. Note the increase in fat following the cystine feeding. Perlman, Stillman and Chaikoff[20] have recently shown that methionine, cystine, and cysteine accelerate the phospholipid turnover in the liver. This may be an explanation for the high fat content of the milk when cystine is fed. According to Ross,[17] this change in composition of the milk does not occur with prolactin administration to human beings. Prolactin

had no effect on the fat, protein, or ash content of the milk. On the eighty-sixth day, tetany and engorged breasts were produced by increasing the cystine fed. The condition again was relieved by using the breast pump. Cystine administration was then stopped and the breasts were practically dry two weeks later.

TABLE I. MILK ANALYSIS—CASE 4

DAYS POST PARTUM	VOLUME C.C.	FAT %	LACTOSE %	PROTEIN %	CYSTINE FED GM.
80	490	2.8	7.2	1.07	0
81	450	3.8	6.8	0.98	2
82	—	—	—	—	2
83	—	—	—	—	1
84	425	3.6	—	—	1
85	—	—	—	—	1
86	505	4.9	6.5	1.20	0
87	465	4.3	6.7	—	0
88	525	4.2	6.9	—	0
89	490	—	—	—	0
98	250	2.2	7.0	1.10	0

COMMENT

All patients showed a response to cystine feeding. Perhaps a much greater response could have been obtained with a combination of endocrine and dietary therapy. However, it is significant to note that whatever the endocrine set-up might have been, the diet therapy had some effect. It is undoubtedly true that the flow of milk is controlled to a great extent by heredity, a sort of individual hormonal pattern relationship. Conditions may be such that the mammary glands do not secrete the maximum amount which is fairly definitely set by heredity. It is this relatively large group of cases that we believe can be helped by dietary therapy. Diet plays a very important role in stimulating the gland to its maximum function. The sulphydryl containing amino acids are the particular dietary elements responsible for this stimulation.

SUMMARY

Multiparas having a history of lack of mammary function were given cystine by mouth. Milk secretion was stimulated in all cases. The analysis of the milk in one case showed an increased fat content following cystine feeding.

REFERENCES

(1) *Ssubotin:* Virchows Arch. f. path. Anat. **36:** 561, 1866. (2) *Voit, C.:* Ztschr. f. Biol. **79:** 136, 1869. (3) *Hoobler, B. R.:* Am. J. Dis. Child. **14:** 105, 1917. (4) *Adair, F. L.:* AM. J. OBST. & GYNEC. **9:** 1, 1925. (5) *Hitchcock, F. A.:* Am. J. Physiol. **79:** 218, 1926. (6) *Daggs, R. G.:* J. Nutrition **4:** 443, 1931. (7) *Wilkinson, P. D., and Nelson, V. E.:* Am. J. Physiol. **96:** 139, 1931. (8) *Smith, H. G., and Seegers, W. H.:* J. Nutrition **7:** 195 and 209, 1934. (9) *Mapson, L. W.:* Biochem. J. **26:** 970, 1932. (10) *Nakahara, W., Inukai, F., and Ugami, S.:* Science **87:** 372, 1938. (11) *Daggs, R. G., and Tomboulian, R. L.:* J. Nutrition **9:** 581, 1935. (12) *Daggs, R. G., and Lidfeldt, V. S. M.:* Ibid. **15:** 211, 1938. (13) *Wright, L. D., and Haag, J. R.:* Ibid. **17:** 263, 1939. (14) *Haag, J. R., and Wright, L. D.:* Ibid. **19:** 563, 1940. (15) *Harding, T. S., and Cary, C. A.:* Proc. Soc. Exper. Biol. & Med. **23:** 319, 1925-26. (16) *White, A., Catchpole, H. R., and Long, C. N. S.:* Science **86:** 82, 1937. (17) *Ross, J. R.:* Endocrinology **22:** 429, 1938. (18) *Curtis, A. C., Newburgh, L. H., and Thomas, F. H.:* Arch. Int. Med. **39:** 817, 1927. (19) *Hartwell, G. A.:* Biochem. J. **22:** 1212, 1928. (20) *Perlman, I., Stillman, N., and Chaikoff, I. L.:* J. Biol. Chem. **133:** 651, 1940.

STUDIES ON THE PRESERVATION OF PLACENTAL BLOOD*

JOHN SCUDDER, M.D., CHARLES R. DREW, M.D., AND
VIRGIL G. DAMON, M.D., NEW YORK, N. Y.

(From the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University, and the Sloane Hospital for Women)

THE first reference to the use of placental blood for transfusions is found in an article by Rubin[7] which appeared in 1914. Later, reports of its successful use were published by Malinovsky and co-workers[6] in 1934, Bruskin and Farberova[3] in 1936, and Stavskaya[11] in 1937.

The present rather widespread use and investigation of the method followed the report of Goodall, Anderson, Altimas, and MacPhail[4] in 1938.

The purpose of this present investigation is threefold: to ascertain again what are some of the normal constituents of placental blood, to determine whether there is a loss of intracellular potassium, and to compare the Russian preservative with the accepted sodium citrate solution.

METHODS

Potassium was analyzed by the modified argenticobaltinitrite procedure.[8, 12] Cell volume was determined by the hematocrit.[8] The specific gravity of plasma was measured by the falling drop technique of Barbour and Hamilton,[2] from which data the total plasma protein concentration was calculated.[13] The normal values are presented in Table I.

TABLE I. NORMAL VALUES FOR PLACENTAL BLOOD

NUMBER	CELL VOLUME IN PER CENT	PLASMA SPECIFIC GRAVITY	PROTEINS GRAMS PER CENT	MILLIGRAMS PER CENT		
				PLASMA POTASSIUM	WHOLE BLOOD POTASSIUM	CELL POTASSIUM
1	53.9	1.0250	6.16	22.5	235	417
2	68.0	1.0261	6.53	21.3	279	400
3	66.0	1.0280	7.18	27.2	279	409
4	51.9	1.0250	6.16	26.4	225	408
5	50.1	1.0250	6.16	21.3	242	460
6	48.4	1.0231	5.51	26.2	208	401
7	51.5	1.0276	7.04	19.1	211	392
8	58.6	1.0264	6.63	23.7	227	370
Average	56.1	1.0258	6.42	23.5	238	407

In the first six experiments done in 1938, placental blood was mixed with various preservatives and tested. The plasma potassium ranged from 45 to 214 mg. per cent at the end of forty days. No conclusions could be made from this series.

Subsequently, the shape of the flask, the concentration of carbon dioxide, agitation, and hydrogen ion concentration, as well as the selection of the preservative, came to be appreciated as a few of the factors limiting potassium diffusion.[8-10]

With this added knowledge, a controlled experiment was carried out. Two identically shaped cylinders, with ground glass stoppers, capable of holding 42.8

*This study was made possible by a grant from the Blood Transfusion Betterment Association, New York.

c.c. were used to collect the placental blood. In one, 21.4 c.c. of the I. H. T.* solution recommended by Goodall and his co-workers[4] was added to an equal quantity of blood. The anticoagulant was made up according to the formula of Bagdassarov[1] and consisted of sodium chloride, 7.0 Gm.; sodium citrate, 5.0 Gm.; potassium chloride, 0.2 Gm.; and magnesium sulphate, 0.004 Gm. in one liter of distilled water. In the other, 4.2 c.c. of a 3.5 per cent sodium citrate solution was added to 38.6 c.c. of blood to fill the container.

At the time of collection, a 5 c.c. portion was secured in an heparinized hematocrit tube. This served for the initial determination; its analysis revealed:

Hematocrit	58.6% cells 41.4% plasma
Plasma specific gravity	1.0264
Total plasma proteins	6.63 Gm. %
Plasma potassium	23.7 mg. %
Whole blood potassium	227.0 mg. %
Cell potassium (calculated)	370.0 mg. %

After collection, the blood was stored in an electric refrigerator at 4° C. Samples were removed and tested with the results as tabulated in Table II.

TABLE II. COMPARISON OF OUTWARD DIFFUSION OF POTASSIUM IN PLACENTAL BLOOD STORED IN DIFFERENT PRESERVATIVES AT 4° C.

DATE	DAY OF STORAGE	MILLIGRAMS OF POTASSIUM IN PLASMA OF 100 C.C. OF BLOOD	
		I. H. T. SOLUTION	SODIUM CITRATE
8/17/39	0	9.8	9.8
8/19/39	2	33.4	32.5
8/26/39	9	68.9	55.9
9/ 2/39	16	88.6	57.1
9/ 9/39	23	107.5	77.2
Details of the experiment:			
Volume of cells		12.54	22.60
Volume of preservative		21.40	4.20
Volume of plasma		8.86	16.00
Total		42.80 c.c.	42.80 c.c.
Internal cylinder diameter: 1.8 cm.			

DISCUSSION

These findings indicate that the cell volume is approximately 22 per cent higher in placental blood than in that of the adult male; 37 per cent higher than in that of the adult female, and from 50 to 60 per cent higher than that of the reported average[5] for mothers at term.

The specific gravity of the plasma and plasma proteins are approximately 10 per cent lower than the values found in normal adults.

The cell potassium is within normal limits, the whole blood values 25 per cent higher, and the plasma values 41 per cent higher than those found in adults.

CONCLUSIONS

1. The cell volume of placental blood is approximately 50 per cent higher than that of the mother, and 22 per cent higher than that of a normal adult male.

*Central Institute of Hematology and Transfusions of Moscow.

2. The total proteins are less in placental blood than in normal adult blood.

3. The increase in concentration of plasma potassium ion is reconfirmed.

4. The rate of potassium diffusion from the placental blood cells is of the same order as adult blood.

5. These potassium diffusion studies indicate that a final concentration of 0.35 Gm. per cent sodium citrate in preserved blood is a superior preservative to the more complex Moscow I. H. T. solution.

REFERENCES

(1) *Bagdassarov, A.:* Sang **11:** 466, 1937. (2) *Barbour, H. G., and Hamilton, W. F.:* J. Biol. Chem. **69:** 625, 1926. (3) *Bruskin, Y. M., and Farberova, P. S.:* Sovet. vrach. zhur. **20:** 1546, 1936; abst. J. A. M. A. **107:** 2098, 1936. (4) *Goodall, J. R., Anderson, F. O., Altimas, G. T., and MacPhail, F. L.:* Surg. Gynec. Obst. **66:** 176, 1938. (5) *Goodall, J. R., and Gottlieb, R.:* Canad. M. A. J. **35:** 50, 1936. (6) *Malinovsky, M. S., Smirnova, L. G., Bayavshinova, M. S., and Tarzanova, V. G.:* Sovet. khir. **7:** 179, 1934. (7) *Rubin, G.:* New York M. J. **100:** 421, 1914. (8) *Scudder, J.:* Shock: Blood Studies as a Guide to Therapy. Philadelphia, 1940, J. B. Lippincott Company. (9) *Scudder, J., Drew, C. R., Corcoran, D. R., and Bull, D. C.:* J. A. M. A. **112:** 2263, 1939. (10) *Smith, M. E., Tuthill, E., Drew, C. R., and Scudder, J.:* J. Biol. Chem. **133:** 499, 1940. (11) *Stavskaya, E.:* Novy khir. arkhiv. **37:** 72, 1937; abst. J. A. M. A. **108:** 1226, 1937. (12) *Truszkowski, R., and Zwemer, R. L.:* Biochem. J. **31:** 229, 1937. (13) *Weech, A. A., Reeves, E. B., and Goettsch, E.:* J. Biol. Chem. **113:** 167, 1936.

THE EFFECT OF A SALT POOR DIET DURING PREGNANCY UPON THE DURATION OF LABOR

WILLIAM POMERANCE, M.D., AND ISIDORE DAICHMAN, M.D., F.A.C.S.,
BROOKLYN, N. Y.

EVER since the importance of a salt poor diet during pregnancy as a means of reducing the incidence of toxemias of pregnancy, especially eclampsia, was demonstrated, various reports[1-5] have appeared in the foreign literature concerning the effect of such a diet upon the duration of labor. Most reports evidenced a definite reduction in the duration of labor when such a restriction in diet was enforced in the last weeks of pregnancy. It was following one such report that one of us (W. P.) decided to place his private patients on such a regime.

While the reports in the literature concerned themselves with salt restriction in the latter weeks of pregnancy, it was decided to encourage the restriction of salt in the diet of these pregnant patients soon after the disappearance of the nausea and vomiting of the early months of pregnancy. This was done because of the difficulty in having ambulant patients do away with an element of their diet to which they were thoroughly habituated; it was thus felt that certainly during the latter two months of pregnancy the patient would have learned to accept such a salt poor diet. Likewise the testing was limited to private patients since many ward patients do not present themselves for prenatal care until late in pregnancy, and because less control can be exerted over such clinic patients than over private patients. The patients were not chosen

for any particular reason, but were taken consecutively. The restriction in diet was accomplished by having the patient desist from cooking her food with salt and from seasoning the food with salt at the table.

The results seemed to be so striking that it was felt that these should not suffer from the lack of an adequate control. Therefore, these results were compared with a similarly sized consecutive series of private patients (I. D.) of about the same social and economic class, and delivering during approximately the same period. And further the same changes in dietary regimen of pregnancy were then commenced in the private patients of the other author. All of the patients were delivered in the same hospital; and the hospital records were used in computing the duration of labor. Any personal interest in the results were thus removed since the computations were made from figures obtained by internes or residents (who were not aware of any study being in progress) in their histories; the same internes were involved since the patients delivered during the same period, thus removing any possible differences due to interpretation of the answers to the question "When

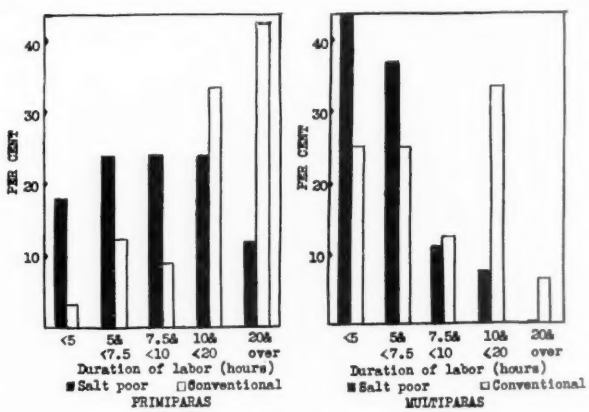


Fig. 1.

did your labor begin?" This is a question often difficult to decide since so many of us find difficulty in deciding "what is labor." If any error existed as to the decision when it actually began, it was approximately the same for all the cases involved. Likewise, because of the difficulty of deciding the end of the first stage of labor, the total duration of labor was taken for comparison, although it was fully realized that the effect of a salt poor diet would *probably* be on the first stage only.

RESULTS

There were 46 patients in the original group of patients on a salt poor diet, including 29 primiparas and 17 multiparas. The average lengths of labor were 9.6 hours and 6.5 hours, respectively. In the control series there were 49 patients, 33 primiparas and 16 multiparas; the average lengths of labor were 22.9 hours and 9.0 hours, respectively. In the second group (I. D.) on a salt poor diet, there were 32 patients, 22 primiparas with an average labor of 10.4 hours, and 10 multiparas with an average length of labor of 4.7 hours. If we add both salt poor

groups together, we have 78 cases: 51 primiparas with an average length of labor of 9.9 hours and 27 multiparas with an average length of labor of 5.8 hours. These results are tabulated in Table I.

TABLE I

	PRIMIPARAS		MULTIPARAS	
	NO.	HOURS-LABOR	NO.	HOURS-LABOR
Salt poor Group I	29	9.6	17	6.5
Salt poor Group II	22	10.4	10	4.7
Salt poor Total	51	9.9	27	5.8
Conventional Diet	33	22.9	16	9.0

These results are better demonstrated graphically and when broken up as in Fig. 1.

From these it can be seen that two-thirds of the primiparas on salt poor diets delivered in less than ten hours, while only one-fourth on conventional diets did likewise. And similarly over four-fifths of the multiparas on salt poor diets delivered in less than 7.5 hours as compared with one-half on conventional diets who did the same.

DISCUSSION

Many factors, ranging from the psychic state of the individual to the size and shape of the pelvis, are determinants of the duration of labor in any case. It was for this reason that the limitations described above were placed upon the study made; it was felt that only in this way could many of these factors involved be approximately the same for the two series compared. No effort was made to determine either the degree of cooperation of the patients (the importance of the diet was stressed at almost each prenatal visit subsequent to the starting of the restriction) or the correlation of such cooperation with the duration of labor. Similarly, it was felt that possibly some of the patients on conventional diets had a relatively salt poor diet as a personal custom.

The foreign reports on this subject also speak of the reduction of the intensity of the labor pains as a result of the salt poor diet. No attempt was made to evaluate this point since it appeared to us that such an evaluation was fraught with the possibility of great error, there being no point of comparison for each patient. It would seem almost a priori that a patient having ten hours of pain would describe her pain as being less intense than one having twenty hours of pain of a similar character. Likewise no attempt is made to suggest a reason for this phenomenon of reduction of duration of labor: whether it is the reduction of the fluid content of the musculature of the uterus, the greater softening of the lower segment of the uterus, a lowering of the threshold of the consciousness of uterine contractions, thereby decreasing the conscious duration of labor, or the greater frequency of Braxton Hicks' contractions resulting in more dilatation of the cervix prior to the onset of labor, or

any other mechanism that may be thought of, is not known. Without some definite experimental proof of any of the above, it would be an idle effort to choose one over the other.

As to the possibility of any contraindications to such a diet, Hammarsten[6] states that "man needs very little mineral matter and this in general is to be obtained from the daily food, since the latter contains a greater quantity than is required by the human body." The sole exception would seem to be sodium, which is necessary to the diet of people living almost exclusively on vegetables (especially potatoes, etc.) rich in potassium, which has a tendency to drive sodium out of the body. This would seem to be of not such great importance during pregnancy when there is a tendency to retain sodium in the body. The universal use of salt as a condiment by all classes, unconsciously leads to the habit of using it in excess of normal requirements which are variously stated as from 2 to 4 Gm. daily.[7] According to Fitch,[8] sodium and chloride equilibrium can apparently be maintained on less than one-fourth the amount of salt ordinarily consumed. Many of the ordinarily consumed foods are high in sodium: bread, butter, milk, cheese, egg white, lima beans, carrots, olives, raisins, spinach, wheat bran, clams, oysters, and meat.[9] These are some of the staples of the diets of our community, and a marked inroad in the consumption of many of these would be necessary before the total requirements of the body would be interfered with.

CONCLUSION

It would seem quite evident, from a study of 78 cases on a salt poor diet and adequately controlled, that there is a definite reduction in the duration of labor following the use of such a diet during pregnancy.

NOTE: Since the preparation for publication of these results was begun, a paper appeared in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY for May, 1940, on the same subject by Ernest E. Wadlow with essentially similar results.

REFERENCES

(1) *Reeb, M., and Israel, L.:* Gynec. et obst. **27:** 193, 1933. (2) *Israel, L.:* Gaz. d. hôp. **106:** 591, 1933. (3) *Lambert, G.:* Zentralbl. f. Gynäk. **59:** 2598, 1935. (4) *Karpati, J.:* Ibid. **59:** 2601, 1935. (5) *Reeb, M.:* Gynec. et obst. **38:** 321, 1938. (6) *Hammarsten, O.:* A Textbook of Physiological Chemistry, New York, 1912, John Wiley & Sons, Inc., p. 843. (7) *Bridges, M. A.:* Dietetics for the Clinician, Philadelphia, 1937, Lea & Febiger, p. 85. (8) Fitch, W. E.: Dietotherapy, New York, 1922, D. Appleton-Century Co., **2:** p. 348. (9) *Bridges, M. A.:* Dietetics for the Clinician, Philadelphia, 1937, Lea & Febiger, p. 103.

140 EIGHTH AVENUE.

Kronfeld, Rudolf: Ovarian Dermoid Containing Teeth, J. Dent. Research **19:** 145, 1940.

Teeth in ovarian dermoid cysts are not particularly rare but in contrast to Japanese, and especially German medical literature, but little has been published on this problem in this country. In a brief review of foreign literature the writer points to the fact that in any ovarian cyst, if they can be identified as right or left teeth, all of them always belong only to one side of the body.

In the case reported here the dermoid contained three erupted teeth and one tooth germ, outside of bone, hyaline cartilage, nervous and brain tissue, cysts, pigment cells, fat tissue, and skin with hairs, and sebaceous and sweat glands.

HUGO EHRENFEST.

AN ACCURATE ROENTGENOLOGIC METHOD FOR DETERMINING PELVIC DEPTH

RUPERT E. ARNELL, M.D., WILLIAM F. GUERRIERO, M.D.,
NEW ORLEANS, LA., AND JAMES B. IRWIN, M.D., SAN FRANCISCO, CALIF.
(From the Departments of Obstetrics and Gynecology of the School of Medicine of Louisiana State University and Charity Hospital of Louisiana, New Orleans)

IT HAS long been recognized that the distance from the plane of the inlet to the plane of the ischial spines and the distance from the latter point to the plane of the outlet, reveal wide individual variations. For that reason the terms "shallow pelvis" and "deep pelvis" have acquired a definite clinical significance. For the same reason the accurate determination of the distance which the fetus must descend through the bony pelvis is a matter of considerable clinical importance not only in patients who require operative intervention but also in patients who deliver spontaneously.

It is curious that, notwithstanding the admitted importance of a knowledge of the depth of the true pelvis, no satisfactory precision method for determining it seems to have been suggested. Textbooks of obstetrics usually state that pelvic depth can be estimated from the impressions derived from vaginal examination, but this is in no sense a satisfactory method. Furthermore, such impressions are fundamentally erroneous because of the introduction of the personal equation, quite aside from the fact that such value as they possess is entirely dependent upon the clinical experience of the examiner.

So far as we have been able to determine, Schuman[1] has published the only method on record in the literature for obtaining the measurement of pelvic depth. By his method the perpendicular distance from the inferior surface of the ischial tuberosity to the superior border of the ramus of the pubis is determined by means of an ordinary pelvimeter. In his cases the average clinical measurement of the pelvic depth was 11.5 cm. and the average bony measurement, after due allowance for pubic and gluteal soft tissues, was 10.5 cm. Schuman emphasized the importance of this measurement and stated that increased pelvic depth was the most important characteristic of the male, funnel, or high assimilation pelvis.

The method for determining pelvic depth which we are describing in this communication was devised in the course of an investigation of the clinical value of the Ball technique of pelvicephalography. Following preliminary studies,[2] we analyzed 503 selected cases[3] studied by this method in regard to pelvic architecture, pelvimetry, fetometry and fetopelvic relations. Our conclusion was that when due regard was paid to clinical considerations and to those intangible factors which, even more than mechanical considerations, determine the course of labor, Ball pelvicephalography is a very useful procedure, in that it warns the obstetrician, accurately in most instances, of possible mechanical risks and difficulties to be expected during labor and at delivery.

The method for determining pelvic depth, which is proposed herewith, should be accepted with precisely the same reservations and qualifications. That is, we consider it an accurate method which supplies valuable data. We are not proposing it as a substitute for clinical observation and judgment.

TECHNIQUE

Pelvic depth can be determined from the pelvicephalograms made for the purposes listed above, no special additional exposures being required. Three sites were used for the determinations, the forepelvis, the posterior-pelvis, and the pelvic canal, and

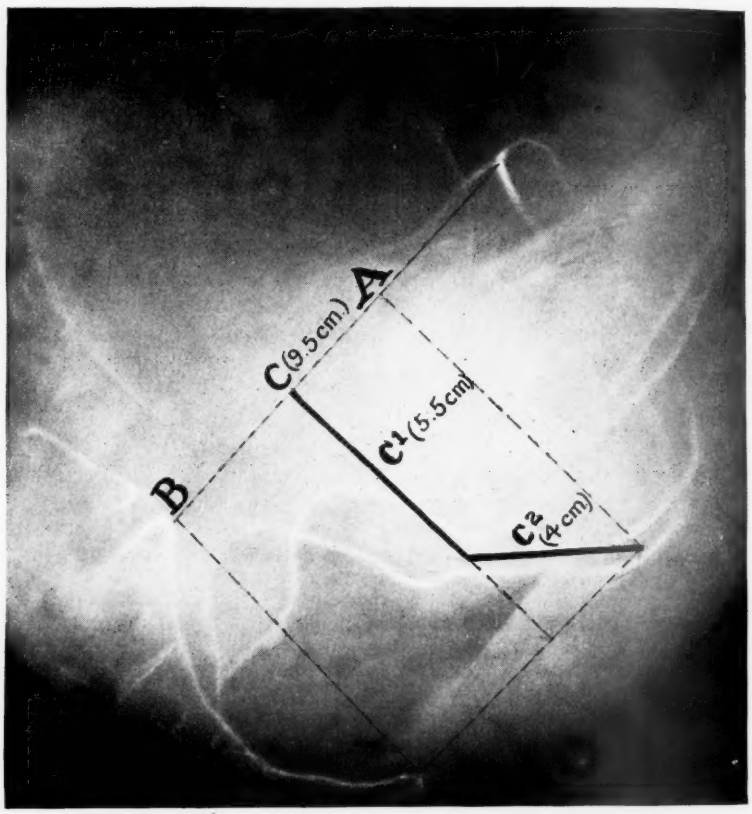


Fig. 1.—Pelvicephalogram of primipara with shallow pelvis. Note the shallowness of the pelvis (line *C*) and the difference in distance from the inlet to the spines (C_1) and from the spines to the outlet (C_2). The patient delivered a child weighing 7¾ pounds after a two-hour labor.

it was determined by comparative studies that measurements of the pelvic canal furnished the most accurate and valuable data. Whatever site is used, the measurements are made from the lateral film. The anterior film furnishes the correction factor; since all measurements on the lateral film are in the same plane, the same correction is necessary as is necessary in the estimation of the true conjugate.

1. When the forepelvis is used as the site of measurement, the pelvic depth is represented by a line perpendicular to the true conjugate and drawn from the upper margin of the symphysis pubis to the plane of the pelvic outlet (Figs. 1 and 2, line *A*). This measurement closely approximates the pubotuberous measurement, which can be determined manually and which usually represents the shortest vertical height of the pelvis. The clinical value of a knowledge of the depth of the forepelvis

is lessened by the fact that the fetal head does not descend in this far anterior location. The measurement also does not make any correction for the changes in depth which usually occur in the posterior aspects of the pelvis and which occur more commonly in the male type of pelvis.

2. When the posterior pelvis is used as the site of measurement, the pelvic depth is represented by a line drawn from the sacral promontory to the sacrococcygeal articulation (Figs. 1 and 2, line *B*). This measurement is dependent upon the length and curvature of the sacrum, and therefore is the chord of the arc described by the sacrum rather than the true pelvic depth. The measurement is of even less value, furthermore, because the inclination of the sacrum is of more importance than its height. Two pelves, for example, may have sacra of equal length and curvature. In one the sacrum is directed backward and the pelvis is therefore adequate. In the other, the sacrum points sharply forward, encroaching on the outlet and thus producing an inadequate pelvis.

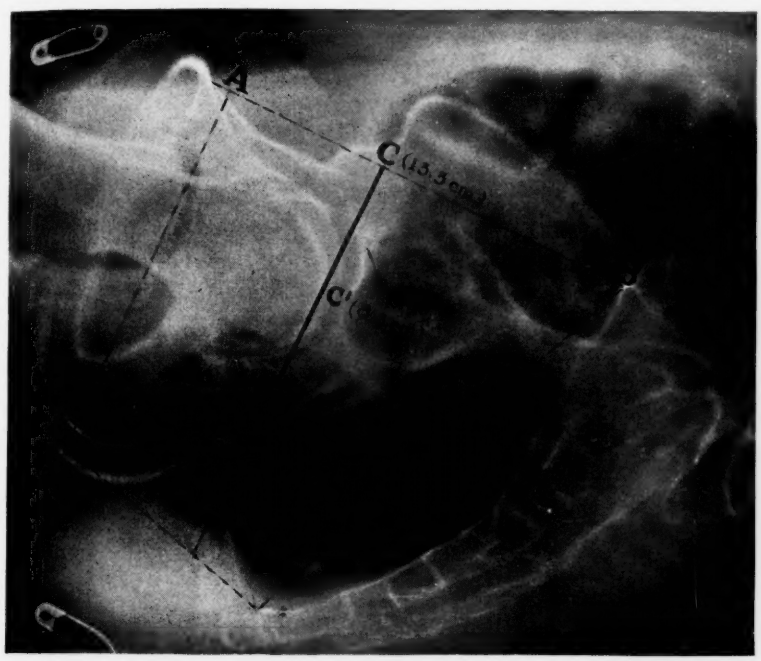


Fig. 2.—Roentgenogram of the pelvis of a primipara. Note that the pelvic depth (line *C*) is considerably greater than the pelvic depth in Fig. 1. Note also the increased depth from the forepelvis to the posterior pelvis. Fourteen months before this study was made the patient delivered a child weighing seven pounds after a sixteen-hour labor.

3. When the pelvic canal is used as the site of measurement, two determinations must be made. A perpendicular line is drawn from the true conjugate to the midpoint of the diameter between the ischial spines (Figs. 1 and 2, line C^1). A second line is drawn from the midpoint of the biischial spinous diameter to the midpoint of the transverse diameter of the outlet (Figs. 1 and 2, line C^2). The total depth of the pelvic canal (*C*) is the sum of line C^1, which is the distance from the inlet to the midplane of the pelvis, and line C^2, which is the distance from the midplane to the pelvic outlet.

The third of these measurements, in our opinion, is a more accurate index of pelvic depth than either of the first two because it represents the approximate distance the fetal head must descend through the true pelvis. This measurement also furnishes useful information concerning the relationship of the midplane (spines) to the inlet and outlet of the pelvis.

DATA IN 100 CASES

In 100 consecutive cases studied by the method described, the average pelvic depth was 11.97 cm., with 15 cm. and 8.2 cm. the upper and lower limits. The difference between the deepest and shallowest pelves, 6.8 cm., is surprisingly wide. The great majority of cases, 72, measured from 10.1 to 13.1 cm. The pelvic depth was between 8.1 and 9 cm. in 4 cases; between 9.1 and 10 cm. in 5; between 10.1 and 11 in 19; between 11.1 and 12 in 31; between 12.1 and 13 in 22; between 13.1 and 14 in 12; and between 14.1 and 15 cm. in 7 instances.

In addition to making information available as to total pelvic depth, the method we have proposed supplies data concerning the relationship of the ischial spines to the inlet and outlet of the pelvis. This relationship is subject to marked variations. In the 100 cases studied, the average distance of the spines from the pelvic inlet was 7.3 cm., and the average distance from the spines to the pelvic outlet was 4.67 cm. Greater variations occurred in the relationship of the spines to the inlet than to the outlet.

This relationship is important because the station (degree of descent) of the presenting part is determined from these land marks. Generalizations as to station are not satisfactory, because individual variations make it necessary to individualize in each case the degree of descent of the presenting part. If the ischial spines are a relatively short distance from the inlet, for instance, as when C^1 is less than usual (Fig. 1), the presenting part may not actually be engaged when it reaches the level of the spines. On the other hand, when C^1 is greater than usual (Fig. 2) and the ischial spines are relatively far from the inlet, the presenting part, when it reaches this plane, would be deep in the pelvis and well engaged.

The accuracy of the method has been checked on cadaveric material, and the errors revealed have been consistently less than ±0.15 cm. We are presently engaged in correlating the type of labor and delivery with the factor of pelvic depth in the 100 cases studied and shall report these data elsewhere.

SUMMARY AND CONCLUSIONS

1. An accurate determination of pelvic depth is a valuable adjunct to pelvic measurements as they are now taken. Data concerning the relationship of the ischial spines to the planes of the inlet and outlet of the pelvis are also of value.

2. A precision method of securing these data is afforded by the use of Ball pelvicephalograms. The method of securing the measurements is described.

3. The average depth of the pelvic canal in 100 consecutive cases was 11.97 cm. The variation was considerable, the shallowest and deepest pelves being, respectively, 8.2 cm. and 15 cm. in depth.

4. In the same 100 cases the average distance from the pelvic inlet to the ischial spines was 7.3 cm., and from the ischial spines to the outlet 4.67 cm. Considerable variations occur in the distance from the inlet to the spines, but the variations in the distance from the spines to the outlet are less marked.

REFERENCES

(1) *Schuman, W.:* Am. J. Obst. & Gynec. **28**: 497, 1934. (2) *Guerriero, W. F., and Smith, W. L.:* New Orleans M. & S. J. **91**: 299, 1938. (3) *Guerriero, W. F., Arnell, Rupert E., and Irwin, J. B.:* South. M. J. (In press.)

CHORIONEPITHELIOMA OF THE UTERUS

With Thyrotoxicosis, Pronounced Hormone Titer, and Death From Intra-Abdominal Hemorrhage

Irving Smiley, M.D., and Alfred B. Clements, M.D.,
New York, N. Y.

(From the Department of Gynecology and Pathology of The Bronx Hospital)

MRS. F. K., aged 27 years, was admitted to the Bronx Hospital on the service of Dr. Smiley with the following history: She had been married 7 years, and had had a spontaneous delivery of a living child five years ago. In August, 1933, she complained of vaginal bleeding, of about two weeks' duration, after having skipped one period, and, on the thirtieth of that month, she aborted. (It was only after she had been in the hospital ten days during her present illness that we were able to ascertain the fact that the material expelled at that time had resembled a cluster of grapes, and that the ambulance surgeon who was called to transfer her to the hospital had called it a mole.) She was removed to one of the neighboring hospitals where she remained for a period of ten days. Because of the continuous bleeding, she was curetted. The curettings consisted of practically normal endometrium. The bleeding stopped, and she was discharged several days later apparently cured, although somewhat pale and underweight.

Her general condition gradually improved, and her menstrual periods returned to a normal condition by October, 1933. She gained weight and considered herself perfectly normal in all respects.

Present Illness.—Her last menstrual period was June 29, 1934. She had complained of frequent attacks of headaches, nausea, and vomiting in the early part of August, 1934. In the latter part of that month there was slight staining which lasted for about two days. Becoming quite apprehensive about the possibility of another abortion, she sought medical advice and was assured that she was pregnant and that, with rest in bed, the pregnancy would continue. The slight bleeding did stop and she felt well until the morning of Sept. 6, 1934, or about nine weeks after the cessation of her last period, when she was awakened by a severe attack of vomiting. Within a short time she lost the power of speech, followed soon after by complete loss of motion of both right extremities. She became semicomatose, in which condition she was removed to the same hospital where she had been curetted. She improved somewhat under general care, regaining some power of motion in the hand and foot and was able to understand what was said to her, though still unable to speak.

She left the hospital on Oct. 6, 1934, of her own volition. The hospital diagnosis (communication) at the time of her discharge was "cerebral hemorrhage of a nontraumatic origin and pregnancy of two months' duration." The following positive findings were reported: (1) Positive Aschheim-Zondek test. (2) Spinal fluid examination showed the presence of xanthochromatism with increased spinal pressure. (3) Ophthalmic examination revealed the presence of a slight papilledema of the left eye (2 diopters). X-ray examination of the chest was negative. She remained at home until Oct. 17, 1934, where she was seen by one of us (I. S.) and immediately transferred to the Bronx Hospital.

Physical examination at this time revealed a young, white female, acutely ill, very anemic and showing evidence of loss of weight. The temperature was 100° F., pulse about 140, and respirations 24. There was present a very anxious expression, an inability to talk, and a flaccid paralysis of both right extremities. A marked tremor of the left hand was very prominent.

Examination of the eyes revealed a widening of the palpebral fissures with a marked degree of exophthalmos. There was lagging of downward movement of the upper lids with downward gaze. The power of convergence was poor. Both pupils were dilated, reacted well to light, but sluggishly to accommodation. Both discs were edematous, two diopters elevation in the right and four in the left. The retinal veins were dilated and small hemorrhages were noted around both optic discs. The conclusion was that the patient was suffering from increased intracranial pressure plus definite evidence of an exophthalmic goiter.

Examination of the neck showed the presence of a uniformly enlarged thyroid gland and measurement over the gland was 12 inches (30 cm.). Examination of the chest showed the lungs to be entirely negative to auscultation and percussion. We may add, at this point, that at no time during this illness were there symptoms referable to the respiratory system. The heart was negative except for a persistent tachycardia.

Examination of the abdomen was negative except for the presence of a nontender, movable mass situated in the right lower quadrant immediately above the inguinal ligament.

Pelvic examination revealed a moderately relaxed perineum. The cervix was somewhat hypertrophied, softer than normal and the external os was irregular in outline and freely movable. The uterus was anterior, softer than normal, about the size of a two-month pregnancy and freely movable. To the left of the uterus was readily palpated a nontender, movable mass about the size of a plum. To the right was felt a larger mass which corresponded to the mass felt on abdominal examination and seemed to be about the size of an orange. Neurologic examination revealed a bilateral optic neuritis, right hemiplegia, diffuse, lower, motor neuron involvement as disclosed by the presence of atrophy, loss of the deep reflexes, and a bilateral Babinski. The conclusion reached by the examining neurologist was that we were dealing with a widely diffused, metastatic condition involving the brain and cord and that there was present both upper and lower neuron involvement, one lesion being located in the left motor area and another in the left parietal region.

Laboratory Findings.—Urine, repeatedly negative. Blood: On admission, hemoglobin 73 per cent (Sahli), red blood count, 3,300,000; white blood count, 6,300, of which 76 per cent were segmented neutrophiles. Subsequent examinations showed a steady drop in the red blood cell picture, the hemoglobin falling to 35 per cent on November 6. The red cells showed marked anisocytosis, central achronia, and polychromatophilia. Wassermann and Kahn reactions were negative; blood chemistry showed normal values. Basal metabolism, plus 28 on Oct. 20, 1934, and plus 17 on Oct. 31, 1934.

The electrocardiogram showed the presence of sinus tachycardia with slurring of the QRS complex in all leads and a tendency to right ventricular preponderance. The conclusion was that the patient showed definite evidence of myocardial disease.

X-ray Examination.—In view of the possibility in the differential diagnosis that we were dealing with a case of chorionepithelioma with metastases, an x-ray of the chest revealed, through the lungs, numerous round metastatic nodules of varying sizes, suggestive of chorionepithelioma.

Hormone Findings.—The presence and amount of anterior pituitary-like substance in the urine were determined by the use of a modification of the Aschheim-Zondek test. The titer of the hormone present was estimated quantitatively, and the results obtained may be summarized as shown in Table I.

Friedman tests were carried out on 10 rabbits. Amounts corresponding to 0.01 c.c. of whole urine gave positive reactions in rabbits as compared with 10 to 12 c.c. used in the routine diagnosis of pregnancy. The reaction was much more pronounced than usually seen in normal pregnancies: The ovary resembling a cluster of bright-red cherries. The "blutpunkt" remained conspicuous for more than six weeks following injection. One of the rabbits was laparotomized ten weeks following injection, and it was seen that both ovaries were the seat of

TABLE I. PROLAN DETERMINATIONS

DATE	PATH. NO.	MOUSE UNITS/LITER OF URINE	RESULTS
10/26/34	6482	2,000	Reaction 2 and 3
		3,000	Reaction 2 and 3
		4,000	Reaction 2 and 3
10/31/34	6504	6,000	Reaction 3
		8,000	Reaction 3
		10,000	Reaction 2 and 3
11/ 5/34	6549	1,000,000	Reaction 3
		1,500,000	Reaction 3
		2,000,000	Reaction 3

extensive corpora lutea formation. Such prolonged ovarian effect has, to our knowledge, never been reported previously.

Progress.—Her pulse rate was inconstant, ranging between 120 and 160 per minute, usually remaining about 140. The highest elevation of temperature reached was 101.5° F. and the respirations remained constant, about 24 to 26. She was fairly comfortable until several days before she died, when there were intermittent attacks of nausea and vomiting. There was marked improvement in her ability to use her arm and leg and she made many attempts to speak, succeeding finally in uttering a few words quite clearly. She appeared brighter, more cheerful and there was considerably less vomiting. The measurement of her neck showed a decrease of one-half inch in circumference.

In view of the patient's poor physical state, the involvement of her myocardium as evidenced by the electrocardiogram, the presence of marked hyperthyroidism and constant tachycardia, and the widespread dissemination of the tumor, it was felt that surgical treatment should be deferred. She was therefore transfused and given deep x-ray therapy.

Repeated vaginal examinations disclosed no change in the size of the uterus, total absence of any bleeding, but definite increase in the size of the masses palpated in both fornices. These tumors became irregular in outline, the one on the right reaching almost halfway to the umbilicus.

On November 3, the patient complained of pain radiating from the left shoulder to the elbow associated with abdominal cramps. This improved within twenty-four hours, but returned on November 6, when she became restless and gave the appearance of intra-abdominal bleeding, respirations became labored, and heart-beat very rapid and weak. Within an hour her skin was cold and clammy. The patient became pulseless and died in spite of stimulation. Permission for a post-mortem examination was obtained and a complete autopsy performed within two hours after death (by A. B. C.).

Autopsy Findings.—The relevant necropsy findings were as follows: Upon opening the peritoneal cavity, there was seen approximately 1,500 c.c. of bloody fluid with several large clots in the lateral gutters and behind the liver. The uterus appeared to be enlarged, measuring 9 by 7 cm. in its largest diameters. No tumor or other abnormality was noted on its outer surface. The peritoneal reflection showed no gross pathology. The appearance of the ovaries, however, was very striking. Both were greatly enlarged, nodular, and cystic, the right being greater in its largest diameters than the uterus, measuring 10.5 by 7 cm. The left ovary measured 8 by 6 cm. Both ovaries were very similar in appearance, being the seat of many small and large lutein and hemorrhagic cysts. One of the latter, in the right ovary, measuring 1.5 cm. in its longest diameter, had recently ruptured and was filled with blood clot. This was evidently the source of the blood found free in the peritoneal cavity. Upon opening the uterus, there was found a large, reddish brown, friable mass measuring 5 by 4 cm. which occupied almost the entire body of the uterus but was situated toward its upper and posterior portions. The demarcation of the tumor mass from the uterine wall could be discerned quite clearly. The latter was compressed to a very thin layer, particularly near the upper pole and some-

what laterally, the uterine musculature gradually widening as it approached the cervical canal. A smaller secondary mass, measuring 5 mm., was noted on the anterior uterine wall. The larger uterine tumor lacked the red, infarct-like appearance of the metastatic tumors in the other organs. The small remaining portion of the uterine canal exhibited an edematous, necrotic endometrium.

Both kidneys were the seat of numerous small and large oval encapsulated masses, the largest measuring 1.5 cm. These were dark and hemorrhagic and had the general appearance of fresh infarcts. Branches of the renal vessels reaching these areas appeared to be blocked with tissue resembling the secondary tumors. The central portions of some of these infarcted areas were distinctly necrotic.

The spleen measured 18 by 18 cm. in size and was markedly congested. There were numerous subcapsular, reddish brown, circumscribed areas, measuring 2 to 3 cm. Near one pole there was seen a large hemorrhagic infarct occupying almost one-third of the organ into which could be traced one of the main branches of the splenic vein. This was thrombosed with tumor material which extended into its finest ramifications. In the center of the intact portion of the spleen, there was seen a mass measuring 3 cm. and numerous smaller, irregular areas of hemorrhage. The central zone of each metastatic tumor was necrotic.

The liver was 26 by 17 cm. in size and the seat of several reddish nodules situated chiefly under the capsule and projecting above its surface. These masses varied in size from 2 to 3 cm., were friable and hemorrhagic and the vessels leading to them were occluded by tumor thrombi.

The serosal aspect of the mid-ileum was the seat of 3 firm, hemorrhagic, oval tumor masses, each having depressed centers corresponding to areas of necrosis. Each mass measured approximately 2.5 cm. in its largest diameter and extended through the wall of the bowel. The main branches of the superior mesenteric vessels appeared to be free of thrombi. Six similar, but smaller and more superficial, nodules were scattered on the serosal aspect of other portions of the ileum.

The anterior portions of the bodies of the third and fourth lumbar vertebrae appeared to be softened and hemorrhagic.

The lungs were studded with innumerable small and large dark red nodules, varying in size from a few millimeters to 6 cm., the larger ones being situated near the bases. The masses projected prominently above the surface of the lung. Both lower lobes were so extensively involved that hardly any intact pulmonary tissue remained. Upon section, the nodules were dark red, hemorrhagic, and well demarcated while the intervening, uninvolved tissue appeared quite normal.

The brain exhibited two major areas of hemorrhagic infarction with thrombosis of the lenticulo-striate and lenticulo-optic branches of the middle cerebral artery. The larger area measured 5 by 2.5 cm. and occupied the greater portion of the anterior half of the left cerebral hemisphere. The smaller measured 1.5 by 1.5 cm. and was situated in the left parietal lobe, 2.5 cm. distant from the longitudinal sulcus; Broca's and Wernicke's areas were within the thrombosed sites. The pituitary gland was yellowish in color and measured 1.5 by 0.8 cm.

Microscopic Pathology.—The histopathology was essentially that of a rapidly growing tumor, relatively small at the point of inception in the uterus but infiltrating vascular channels and producing extensive local and metastatic thrombotic and hemorrhagic areas. The uterine tumor exhibited narrow and broad irregular anastomosing strands of acidophile syncytial cells, some multinucleated, and islands of smaller, paler-staining Langhans cells with more definite cell outline. The stroma was sparse and irregularly distributed and deposits of fibrin were interspersed between the masses of actively growing neoplastic tissue. There appeared to be a definite zone of productive inflammation in and about the strands of invasive tissue. The tendency to vascular infiltration was not marked in the uterine tumor, so that thrombosis and hemorrhagic infarction were much less prominent than in any of the secondary tumors. However, occasional small scattered areas of necrotic tissue might be seen. The musculature was broken up by advancing tumor cells but complete penetration had not as yet occurred. Sections taken from the small

remaining area of what appeared to be intact endometrium adjacent to the tumor mass revealed extensive necrosis with evidence of local extension of the neoplastic process. No normal endometrium could be seen nor definitely identified.

Sections from the lung exhibited extensive foci of thrombosis, necrosis, and hemorrhage with contiguous areas of exudative, reactive inflammation. The typical picture was a central core of thrombosed, necrotic tissue consisting chiefly of cellular detritus, fibrin, and red cells, outside of which was a sinuous border made up of macrophages capped by a broader, irregular zone of intact neoplastic tissue. The stroma was extremely scant and the adjacent normal pulmonary tissue was atelectatic. Some alveoli were filled with inflammatory exudate. The individual tumor masses were so numerous that comparatively little pulmonary tissue remained intact. In some places one might discern actual invasion of and spread through the alveolar wall with almost complete filling of the air vesicle by tumor cells. More or less hemorrhage accompanied the process in each case (Fig. 1).

Fig. 1.

Fig. 2.

Fig. 1.—Invasion of wall of pulmonary alveolus by tumor tissue.
Fig. 2.—Tumor emboli in kidney.

The liver was the seat of extensive focal and coalescent thrombotic areas with apparently viable tumor tissue, however, always visible at the periphery. In some sections invasion was definitely limited to the portal canal, but this appeared to be merely an early stage of the same process, giving rise to larger areas of coalescent tumor tissue seen elsewhere. Invasion of the vascular channels was very pronounced and, as adjacent lobules were invaded by neighboring tumor masses, the intervening hepatic parenchyma was compressed and atrophic. The sinusoids appeared to be wider than normal and the reticulum more prominent, but this might be more apparent than real by reason of the narrowing of the liver cords. In many places the cells of Kupffer stood out prominently.

The kidney sections exhibited, perhaps, next to the lungs, the most extensive thrombotic areas. One could often discern the hemorrhagic area clearly encompassed by venous wall and not infrequently intramural nests of tumor cells which, in places, had reached the adventitia. Here and there one might note small sheets of syncytium and Langhans cells which appeared to be actively growing through the hemorrhagic mass rather than having been merely caught in its meshes. The apparent absence of any definite stroma suggested its local source of nutrition. The renal parenchyma adjacent to this area was compressed, atrophic, and infiltrated with nonneoplastic wandering cells. Many of the glomerular tufts were completely thrombosed by small emboli of tumor cells so that all one saw was a round or oval area of clear serous material capped at one end by a tiny nidus of tumor tissue. The whole was shrunken away from the parietal layer of the capsule. The affected glomerular beds were several times the size of adjacent normal ones. The interstitial tissue was infiltrated by wandering macrophages (Fig. 2). Invasion of the larger renal vessels by neoplastic cells was also seen, the vessel itself being thrombosed, tumor tissue having apparently penetrated and destroyed the intima. The invading sheet of Langhans and syncytial cells appeared to have been obstructed, temporarily at least, by the media against which it was flattened. The advancing growth then spread in a circumferential fashion, the contiguous muscularis having been thinned out. Infarctions produced as a result of this process were numerous and varied in size from a few millimeters to several centimeters.

The cells of the adrenal cortex were hypertrophic and granular and the nuclei were pyknotic and prominent. The stroma was sparse and, in places, definitely separated by clear spaces from the cell cords. The thyroid presented a rather unusual appearance of large acini distended with colloid with low cuboidal to flattened epithelium alternating with smaller, more cellular, areas practically devoid of colloid. No acinar spurring was noted, and there was a distinct diffusely lymphoid stroma. No necrosis, hemorrhage, or calcific deposits were noted.

The pituitary exhibited numerous large chromophobe cells regarded by Novak and others as characteristic of gestation. In the sections examined, these cells did not appear to outnumber the basophiles which Stockl regards as associated with an increased secretion of the gonadotropic hormone and secondary to the chorionepithelioma. Nor did the chromophobes appear to be greatly in excess over the eosinophiles which are regarded by Philipp as associated with hypersecretion of the pituitary. From a careful examination of many sections, it might be said that the chromophobe cells stand out very prominently by reason of their hypertrophy rather than because of an actual marked increase in their number.

SUMMARY

The above case was one of chorionepithelioma of the uterus with extensive metastatic spread. The thyrotoxic symptoms, the lutein cysts of the ovary, the tremendous hormone titer, and the mode of death by intra-abdominal hemorrhage were but a few of the outstanding features present.

We are indebted to Dr. Joseph Felsen for the pathologic studies and the photomicrographs.

900 Grand Concourse

UNUSUAL COEXISTENCE OF SQUAMOUS CELL CARCINOMA AND CERVICAL FIBROMYOMA*

MALCOLM B. DOCKERTY, M.D., AND JAMES C. MASSON, M.D.,
ROCHESTER, MINN.
(From the Mayo Clinic)

UTERINE fibromyoma and uterine carcinoma both constitute a fair proportion of gynecologic lesions, and it is not surprising that these two conditions are encountered occasionally in combination. According to Martzloff[7] in a study of more than 16,000 cases of uterine fibromyoma, carcinoma of the corpus uteri was present in 2.23 per cent and of the cervix, in 1.5 per cent. However, since cervical fibromyomas constitute but 5 per cent of the entire group and since pedunculation is the exception rather than the rule, the coexistence of squamous cell carcinoma in such a case becomes a matter of extreme rarity. When the malignant process is confined to the stalk of the fibromyoma, we have a combination of circumstances bordering on the unique. In the literature, however, we encountered articles by Bishop,[1] Chisholm,[4] Geller,[5] Princeteau[8] and Stein,[9] describing cases comparable in many respects to the one we wish to report.

REPORT OF CASE

A single white woman, aged 56 years, came to the Mayo Clinic on Feb. 13, 1940; she complained of daily, vaginal, postmenopausal spotting of ten years' duration. For nine years she had followed the counsel of a "friend" who had advised against medical consultation but finally the patient compromised by consulting an osteopath who made a diagnosis of "fibroids" and advised operation.

Examination disclosed an enlarged, somewhat tender uterus which was apparently the seat of multiple fibromyomas. The largest of these appeared to be pedunculated, of cervical origin and somewhat infected. Results of examination otherwise were essentially negative.

At operation on Feb. 17, 1940, a pedunculated fibromyoma that measured 7 cm. in diameter was removed vaginally by one of us (Masson). The unusual condition to be described herein was found on routine fresh frozen sections stained with polychrome methylene blue. Under ordinary conditions, we do not like to open the abdomen for at least a couple of weeks after removing an infected fibroid through the vagina, but on account of the diagnosis of malignancy we felt that we should not wait that long in this case, and three days following the first operation, after thorough sterilization of the vagina, cervix, and raw surface from which the fibroid had been removed, we did a total abdominal hysterectomy. After a convalescence complicated by a mild infection of the upper portion of the respiratory tract, the patient was given a course of roentgen therapy over the pelvis and was dismissed on the thirtieth postoperative day.

Gross features of interest are shown in Fig. 1. Microscopic sections taken through the convexity of the pedunculated growth revealed the usual picture of a hyalinizing fibromyoma with a subacute inflammatory reaction in the superficial layers. Study of a region in the vicinity of the stalk, however, demonstrated a mantling of stratified squamous epithelial cells, somewhat hyperplastic in appearance (Fig. 2). Toward the attachment of the pedicle, the epithelial cells became more irregular in size and shape, giant cell forms were frequently encountered and pronounced cellular activity was evidenced by numerous typical

*Submitted for publication, May 8, 1940.

and atypical mitotic figures. The nuclei were hyperchromatic and contained large nucleoli in every field. One such region is shown in Fig. 3 in which the lesion has reached the stage of epithelioma in situ (Broders). Finally, several

Fig. 1.—Gross specimen showing pedicle of fibromyoma around which the epithelioma was localized.

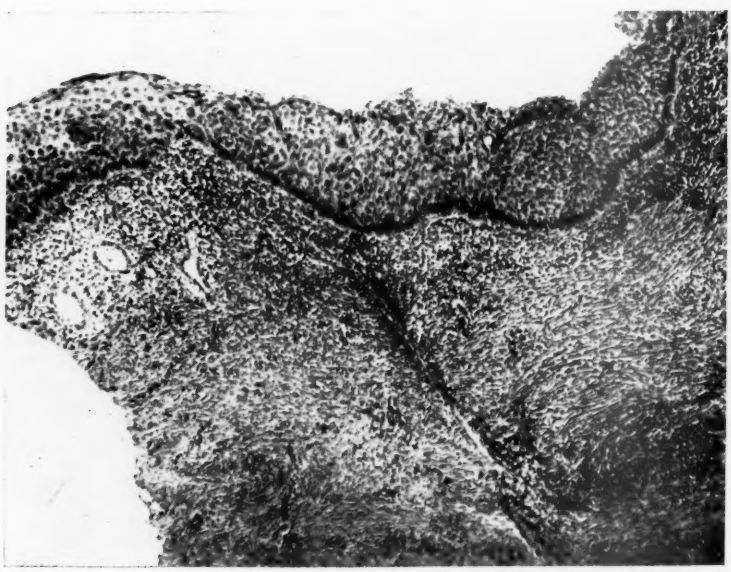


Fig. 2.—Hyperplasia of squamous epithelium covering fibromyoma in vicinity of pedicle (×52).

regions were seen in which the basement membrane was broken and migration superadded to fulfill the most exacting criterion of undoubted malignancy, an invading squamous cell carcinoma, Graded 3 (Fig. 4). Careful examination of the

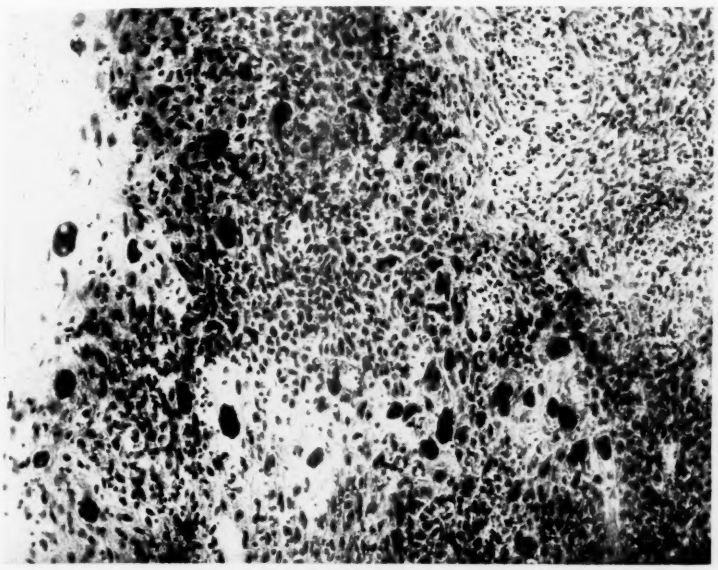


Fig. 3.—Squamous cell carcinoma, Grade 3, in situ. Note hyperchromatic cells with giant nuclei (×95).

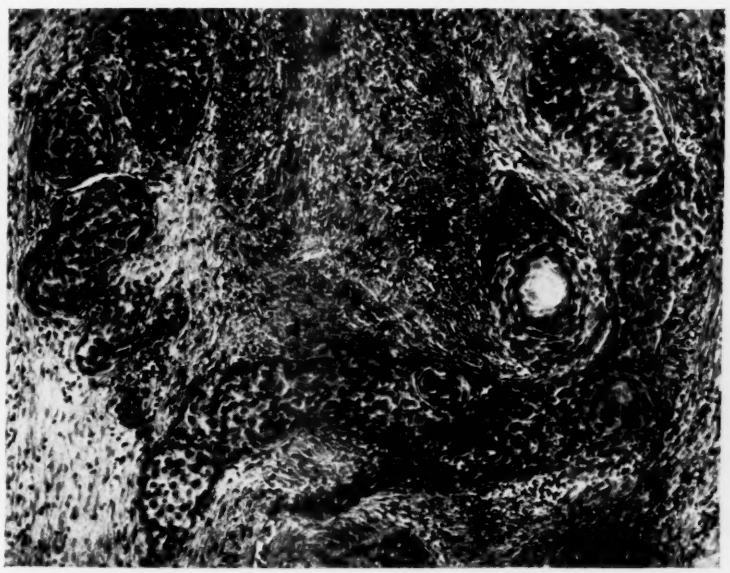


Fig. 4.—Infiltrating squamous cell carcinoma, Grade 3 (×95).

tissue removed at the second operation revealed multiple uterine fibromyomas, cystic endometrium and several small adenomatous cervical polyps. The epithelial lining of the cervix was columnar as far down as the external os (Fig. 5). No trace of carcinoma could be found anywhere in the uterus, the malignant lesion

being peculiarly confined to the stalk of the pedunculated fibromyoma, as already described. The tubes and ovaries were atrophic.

COMMENT

Considerable literature has accumulated on the subject of cellular metaplasia since Küstner,[6] in 1884, called attention to the squamous cell metaplasia occasionally observed in connection with cervical polyps. The roles of trauma, continued irritation and infection have been repeatedly stressed as etiologic factors in the production of this metaplasia which has long been considered in the light of a definitely precancerous condition. Thus, it is pointed out, arise squamous cell carcinomas of the gall bladder and bronchial mucosa, situations in which squamous epithelium is not normally found. It is not surprising, therefore, that metaplasia is encountered frequently in the uterine cervix. Here, trauma, infection, and, frequently, ulceration occur in combination in a region in which squamous cells and glandular epithelium are normally in intimate approximation. It is thus that we attempt to explain in our case the progression through prolonged ulceration, repeated repair and metaplasia to the final stage of malignant neoplasia. The localization of the latter serves merely to emphasize the importance of the etiologic factors and points to the necessity for early treatment of certain benign lesions of the uterine cervix.

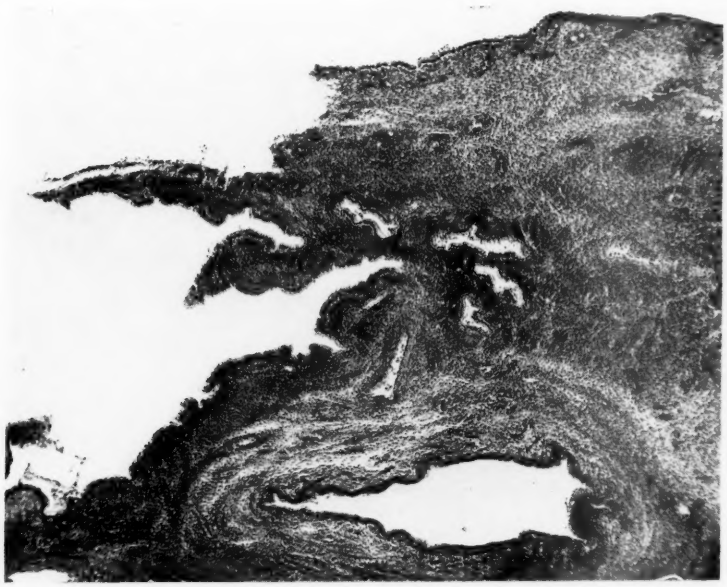


Fig. 5.—Columnar epithelium lining the cervical canal (×32).

SUMMARY

An unusual case of coexistent polypoid cervical fibromyoma and early squamous cell carcinoma is reported. Evidence is adduced that trauma and prolonged chronic irritation led to atypical repair, metaplasia, and eventually to malignant neoplasia.

REFERENCES

(1) *Bishop, Eliott:* Am. J. Obst. & Gynec. **12:** 284, 1926. (2) *Broders, A. C.:* J. A. M. A. **99:** 1670, 1932. (3) *Idem:* Personal communication to the authors. (4) *Chisholm, A. E.:* Practitioner **110:** 320, 1923. (5) *Geller, F. C.:* Zentralbl. f.

Gynäk. **47:** 406, 1923. (6) *Küstner, Otto:* Centralbl. f. Gynäk. **8:** 321, 1884. (7) *Martzloff, K. H.:* In Curtis' Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Company, Vol. 2, p. 838. (8) *Princeteau, René:* Paris méd. **55:** 555, 1925. (9) *Stein, Arthur:* Am. J. Surg. **10:** 136, 1930.

RELEVANT ARTICLES NOT REFERRED TO IN TEXT

(1) *Barthélemy, M.:* Bull. Soc. d'obst. et de gynéc. **25:** 164, 1936. (2) *Counseller, V. S., Cox, F. W., Church, G. T., and Paterson, Susanne J.:* S. Clin. North America **13:** 959, 1933. (3) *Fluhmann, C. F.:* Northwest Med. **26:** 244, 1927. (4) *Findley, Palmer:* Am. J. Obst. & Gynec. **11:** 450 and 519, 1926. (5) *Stone, W. S.:* Surg. Gynec. Obst. **23:** 248, 1916.

ACUTE INTESTINAL OBSTRUCTION COMPLICATING PREGNANCY AND THE POST-PARTUM PERIOD

With a Report of Four Cases

Frederick Weintraub, M.D., and Boris Jaffe, M.D., Brooklyn, N. Y.

(From the Department of Obstetrics and Gynecology and the Department of Surgery, Israel Zion Hospital)

A REALIZATION of the possibility of acute intestinal obstruction occurring as a complication of the pregnant or parturient woman is an indispensable prerequisite to timely diagnosis and rational treatment. In early surgical intervention lies our main hope of effecting some reduction in the high mortality rate exacted by this rare and grave affection. Delay in diagnosis as well as indecision and perilous conservatism in management are all too frequently observable in case reports published both in this country and abroad. The first of the four cases, herein reported, which ended fatally, stimulated the present study and impressed us with the urgent need of readier recognition and more prompt treatment of this complication.

Three of the cases of acute intestinal obstruction during pregnancy occurred in a series of over 32,000 deliveries at the Israel Zion Hospital. The fourth case occurred post partum.

G. G. Bemis found this complication twice in 15,000 obstetric patients at the Woman's Hospital of New York. From 1900 to 1931 the American and British literature contains reports of only 13 cases. Kornfeld and Daichman in 1934 reported one case of volvulus in over 31,000 hospital deliveries and stated that a careful search of the literature failed to reveal any cases reported in this country up to that year. Casagrande in 1936 reported a case of full-term pregnancy complicated by acute intestinal obstruction and stated that two such cases of acute obstruction had occurred in 11,246 hospital cases. Stander in his 1936 revised edition of Williams' *Obstetrics* curtly disposes of intestinal obstruction as follows: "This rare complication of pregnancy should be treated upon general surgical principles." Similar cursory or no consideration is given to the subject in other standard American and British textbooks. In an excellently individualistic article on the "Surgical Complications of Pregnancy," Cosgrove mentions no case of acute intestinal obstruction in 25,000 obstetric patients on his service.

Most of the published reports on this subject are based on the individual author's observation of one, or occasionally two cases. The

unusual experience of having encountered 4 cases of mechanical intestinal obstruction, 3 ante partum and 1 post partum, seems to warrant this report.

CASE REPORTS

CASE 1.—S. S., 41 years of age, para ii, was admitted to the hospital on Sept. 1, 1938. Two spontaneous deliveries, one in 1923 and the other in 1926, and a laparotomy in 1931 for the removal of a left benign ovarian cyst are noted in her history. On admission she was about six weeks before term, and had had irregular labor pains for several hours. Rectal examination disclosed a high breech presentation impressible into the pelvis, and a cervix two fingers dilated and uneffaced. The fetal heart sounds were normal and occasional uterine contractions palpable.

Irregular pains continued until the following morning when, after a few hours of nausea, belching, and retching, there followed an attack of vomiting, and colicky pains in the epigastrium. There was no evidence to indicate a toxemia of pregnancy. By afternoon of the same day all symptoms had spontaneously subsided.

The next day (September 3) marked an episode of recurring epigastric colic, much distention, tenseness, and pain over the epigastrium. The temperature was 102° F. By gastric lavage 1,000 c.c. of dark brown, foul-smelling fluid was recovered. An enema gave a poor result though the patient had had no bowel movement since admission.

Twenty-four hours later (September 4) all symptoms subsided and the abdomen was soft and flat. The rectal temperature was 100° F. Occasional uterine contractions occurred, but the cervix was still two fingers dilated. The impression was constriction by post-operative adhesions of an incomplete type with spontaneous recession.

Since the patient was obviously not in labor, she was transferred on September 5 to the medical service. For the next three days her symptoms remained quiescent and her temperature 99° to 100° F. She was passing some gas and small quantities of feces. On September 8 her temperature rose to 102° F., fecal vomiting suddenly occurred, and the abdomen became moderately distended.

A diagnosis of mechanical intestinal obstruction due to postoperative adhesions was made and operation advised. The family refused consent until the following day. The delay proved unfortunate, for during the subsequent twenty-four hours the patient lapsed into a condition of vasomotor collapse. Transfusions, intravenous glucose, gastric lavage, and other stimulating measures were employed, but she failed to rally sufficiently to attempt surgical intervention.

On the same day after several hours of pains, a male still-born infant was delivered spontaneously by the breech. The following day (September 11) she became comatose, temperature rose to 105° F., and at 11:25 A.M. she died.

Autopsy by Dr. Ravid disclosed partial intestinal obstruction with firm adhesions of the sigmoid to the left uterine cornu. It should be mentioned that after delivery there occurred naturally profound intra-abdominal changes and rearrangement of the intestinal loops and uterus. Hence, the pathologist's report of partial obstruction is at variance with conditions that existed ante partum. The mechanical effects on the intestine resulting from delivery will be more specifically discussed in connection with the second case.

Comment.—This case too well exemplifies the diagnostic pitfalls characterizing acute intestinal obstruction, particularly of the partial type, during late pregnancy. The difficulty was further accentuated by periods of recession of clinical symptoms. The improvement, objective and subjective, following lavage, enemas, and sedatives, is fraught with great danger as it induces a sense of false optimism. To wait for fecal vomiting before venturing a diagnosis is always injudicious and frequently belated. The lower the site of obstruction, the longer will be the interval before such vomiting appears.

CASE 2.—M. B., 35 years old, para ii, had a spontaneous delivery on the day of admission, Feb. 28, 1934. Her pregnancy had been normal. Two previous pregnancies and deliveries had also been normal. During the past ten years occasional episodes of constipation and right lower quadrant pain of varying severity, lasting several days at a time, appear in her anamnesis. A diagnosis of chronic appendicitis had been made.

Before she was removed from the delivery table, it was observed that her right upper and lower abdominal quadrants were considerably distended and tympanitic. This finding persisted through that day and the next; and, on the second day post partum, there occurred in addition to the tympanites, several vomiting spells and moderately severe pain in the right upper and lower quadrants. Her temperature rose to 102° F., pulse 110. On the third day post partum, her symptoms became aggravated. At no time since delivery had she passed any gas or feces.

On the fourth day post partum, fecal vomiting occurred. A diagnosis of obstruction in the transverse colon or its flexures was made. At operation, performed under spinal anesthesia the same day, the cecum, thinned-out and ballooned to the size and shape of a honeydew melon, thrust itself through the incision. The ascending colon was collapsed and surrounded by numerous adhesions in which a long, thin appendix was firmly imbedded. Near the center of the cecum a dark, hemorrhagic area, about one-half inch in diameter, was visible. As soon as the adhesions were liberated, the cecal distention diminished and passage of gas into the collapsed ascending colon occurred. A cecostomy was performed.

During the first five postoperative days, her course was stormy. Improvement was manifest by the tenth postoperative day when spontaneous defecation occurred though the colostomy was draining well. She was discharged twenty-one days after operation. Two months later the cecal fistula was closed surgically.

Comment.—This case demonstrates the possibility of acute mischief during the early post-partum period, arising from adhesions which remained relatively innocuous ante partum. The compression exerted by the enlarging uterus during the course of the pregnancy on the cecum and adherent ascending colon was a gradual process which did not disrupt entirely the patent relationship between these adjacent segments of bowel. It will be recalled that there is a normal tilt to the right and posteriorly of the pregnant uterus which produces increased pressure on the cecum and ascending colon. Immediately following parturition there occurred an extensive and widespread re-arrangement of the intestinal coils and a marked alteration in intra-abdominal and intra-intestinal pressure. As the cecum was suddenly decompressed by the abrupt emptying of the gravid uterus, it is conceivable that an inrush of gas would cause the cecum to distend and probably undergo a certain degree of torsion if there existed any obstruction at a higher level. Such obstruction could readily be brought about at this time by the rendering taut of the many adhesions previously mentioned which, by angulating and fixing the ascending colon with its short mesenteric attachment, would convert its previously patent lumen into an obstructive lesion. The greater the gaseous pressure within the cecum, the more tightly sealed would be the site of obstruction in the fixed ascending colon.

Bearing in mind the modus operandi of the obstruction, it will be understood why the patient's right upper and lower quadrants became markedly distended so soon after emptying of the uterus. In this case the diagnosis should have been made and operative treatment instituted earlier than the fourth day post partum, and before the onset of fecal vomiting since, unlike the previous case, the signs and symptoms were of a progressive nature, in the first place, and, in the second, the post-partum abdomen is more favorable for physical examination than the tense abdomen of late pregnancy or term. However, the opportunity for us to see the patient did not arise until the day of operation.

It is of interest to note that no previous operation had been performed upon this patient. The history of so-called chronic appendicitis or pelvic inflammation in suspected cases of acute intestinal obstruction in the post partum should be given due consideration.

CASE 3.—H. G., 28 years old, para 0, was admitted, when six months pregnant, on Oct. 21, 1939. Her chief complaint was the sudden onset of severe and generalized abdominal pains and frequent vomiting spells, no bowel movement, and no flatus during the preceding twenty-four hours. There was no toxemia. Physical examination revealed a left pararectal scar (ovarian cystectomy, 1937), generalized abdominal tenderness, and moderate distention. The impression was high intestinal obstruction. During the following forty-eight hours her symptoms became intensified.

A laparotomy under spinal anesthesia revealed an omental band wrapped around the lower part of the ileum, tightly constricting it. One foot of distended ileum was deeply cyanotic. Severance of the adhesions and hot applications restored the bowel color and lumen continuity. Uneventful convalescence and discharge from the hospital ten days after operation ensued.

Comment.—In this case, though there was evidence of a former abdominal operative scar, which should have served as a beacon, in the first place, and though there occurred a dramatic onset of all the cardinal symptoms of acute intestinal obstruction, viz., nausea, vomiting, abdominal pain, distention, and constipation, in the second, there followed nevertheless a delay of forty-eight hours before operation was performed.

CASE 4.—J. Y., 32 years old, para i, was admitted on Jan. 20, 1938, when seven months pregnant. In her history appears a record of a right salpingo-oophorectomy and appendectomy nine years previously, and of an umbilical herniorrhaphy four years previously. A normal delivery occurred eight years ago. Her chief complaint was vomiting of seven months' duration. In the first trimester of her pregnancy the vomiting had occurred only in the morning, but thereafter at any time of the day. There had been periods of comparative freedom from vomiting, lasting from a few days to several weeks.

For the entire week preceding hospital admission she had had no bowel movement. During the same week abdominal distress and distention had become marked and vomiting so frequent that it was impossible for her to retain any food. A diagnosis of intestinal obstruction was made. At operation adhesions involving the anterior abdominal wall, omentum, small intestine, and uterus were found. Many intestinal loops were adherent to one another, but the obstruction was caused by several bands constricting the small intestine. The bands were severed, the intestinal coils liberated, and part of the omentum removed. The postoperative course was uneventful and normal delivery at term ensued.

Comment.—The chief complaint in this case was chronic, intermittent vomiting of seven months' duration. Its occurrence in the forenoon, during the first trimester, was interpreted as the ordinary morning sickness of early pregnancy. Precisely when this type of vomiting ceased, and that caused by intestinal obstruction supervened cannot be stated. It may be assumed, however, that this occurred in the fourth month, for it is unusual for ordinary morning vomiting to become aggravated after this period in a patient not suffering from a toxemia. It was then that the vomiting in this case no longer remained limited to the morning but occurred at any period of the day. Furthermore, the abdominal scars and the history of two laparotomies should have directed attention to the possibility of an intestinal complication from adhesions. When one considers also that, during the fourth and fifth months, the uterus encroaches on the abdomen, the mode of production at this time of intestinal obstruction is understandable. During the first trimester, when the uterus is still within the pelvis, it is most rare for adhesions to give rise to serious symptoms. Beginning in the second trimester, the obstructive features persisted in this case until an acute culmination in the seventh month. The enlarging uterus, acting on old adhesions, supplied the mechanical basis for this development.

SUMMARY

1. Because of its rarity and the confusing influence exerted by coexistent pregnancy, acute intestinal obstruction complicating pregnancy is characterized by delay in diagnosis and belated surgical intervention.

2. Three of the cases, herein reported, occurred during the antepartum period in a series of over 32,000 hospital obstetric admissions. The other occurred during the early post partum.

3. From a review of the 4 cases, one is impressed with the important fact that the single fatality of the group occurred in that patient who was not subjected to operation. In the other three cases the relative timeliness of operation was reflected in proportionately favorable results. It is obvious that *pregnancy predicates pernicious procrastination* in the management of this condition.

4. "Primary pregnancy ileus," as defined by previous writers, and its two types are mentioned. In contradistinction to "primary pregnancy ileus," we suggest the designation of "*secondary pregnancy ileus*" for those cases in which pre-existing bands or adhesions are primarily responsible for the obstruction, the mechanical effects of the enlarging uterus being the secondary factor in its production. All of our cases were of the secondary variety.

5. In a gravida who presents symptoms of acute intestinal obstruction, it is of paramount importance to look for the scar of a former laparotomy. In the absence of such scar, however, a history of abdominal or pelvic inflammation may be equally relevant. The commonest operative antecedents have proved to be appendectomy and pelvic operations.

6. Because one or several of the cardinal symptoms of acute intestinal obstruction are so commonly associated with normal pregnancy, they are generally regarded with a complacency that may prove dangerous or even disastrous in the presence of this complication. A discussion of these several symptoms with reference to differential diagnosis is given.

7. Improved maternal and fetal results can be achieved only by early operation. Only the minimal surgical procedure should be carried out that suffices for the relief of the obstruction. A meticulous technique whose objective is to avoid unnecessary disturbance of the pregnant uterus is indicated. Gratuitous surgery is contraindicated.

8. To delay operation during pregnancy in anticipation of spontaneous cure of acute obstruction is to court disaster. Until proved otherwise, each case is *prima facie* one of mechanical obstruction, or, as we term it, "*secondary pregnancy ileus.*"

9. The exceptional instances in which preliminary cesarean section is indicated, are discussed.

We express our indebtedness to Drs. Leo S. Schwartz, Romeo Auerbach, and William L. Wolfson for permission to utilize the foregoing case records.

REFERENCES

(1) *Bemis, G. G.:* Am. J. Obst. & Gynec. **24**: 436, 1932. (2) *Casagrande, J.:* Ibid. **32**: 1058, 1936. (3) *Kornfeld and Daichman:* Ibid. **27**: 768, 1934. (4) *Stander, H. J.:* Williams' Obstetrics, New York, 1936, D. Appleton-Century Co. (5) *Slemons and Williams:* West. J. Surg. **46**: 84, 1938. (6) *Cosgrove, S. A.:* Am. J. Obst. & Gynec. **34**: 469, 1937.

BENIGN POSTIRRADIATION STRICTURE AND PRIMARY CARCINOMA OF THE COLON

JAMES N. STANTON, JR., M.D., AND HAROLD W. JACOX, M.D.,
PITTSBURGH, PA.
(From The Western Pennsylvania Hospital)

WITHIN the past six years attention has been called to the late occurrence of benign strictures of the sigmoid colon and the small intestine following radium and roentgen therapy for cancer of the cervix uteri.[1-3] The interval from irradiation to the appearance of symptoms varied from a few months to as long as eight years. The importance of differentiating between a recurrent malignant condition and a sequela of previous radiation therapy before giving further irradiation or before considering the condition hopeless due to recurrent or metastatic cancer was emphasized.[3]

The patient whose case we report presented such a problem about nine years after she received radiation therapy for a recurrent malignant lesion of the uterine cervix. However, not only a benign stricture of the upper sigmoid colon but also a second primary cancer of the bowel were discovered at laparotomy.

For the patient's past medical history we are indebted to Drs. Thomas S. Cullen and Curtis F. Burnam of Baltimore:

From Thomas Cullen's letter we have the following information: "On May 8, 1930, I saw Miss A. Z. S. of Pittsburgh. The patient was 43 years of age. She began to menstruate at 13 and was regular; flow was moderate, and she had had no pain until the year previous to her coming to see me. Her last period was two weeks ahead of time, and for a few weeks, on the least exertion, she would pass bright red blood from the vagina.

"During the World War she had amebic dysentery.

"On pelvic examination, a cauliflower growth, about 8 cm. in diameter, sprang from the cervix. It almost completely filled the vagina. Fortunately, it was confined to the cervix and was freely movable. The body of the uterus was relatively small. To the right of the uterus was a mass 7 or 8 cm. in diameter, freely movable, and possibly a cyst.

"On May 12, 1930, the patient was operated upon at the Johns Hopkins Hospital. A complete Wertheim operation was done. On the left side the ureter was rather difficult to get at, as there was a little inflammatory thickening in this area. The small ovarian cyst on the right side was removed before the hysterectomy was completed. The patient made a satisfactory recovery.

"The pathologic report was as follows:

"*Specimen.*—The uterus was normal in size and shape. The peritoneal surface was smooth. The cervix was attached, together with a cuff of vaginal mucosa. The latter was pale and smooth and measured about 1 cm. in width. The cervix was a cauliflower-like mass measuring 5.5 cm. in diameter. It was granular and very friable. The larger part of the growth was in the anterior lip, though the posterior lip was also involved. None of the growth seemed to have extended beyond the vaginal cuff.

"The cervix, uterus, left tube, and left ovary were not cut for section, but were saved as a whole for the museum, as a beautiful example of carcinoma of the cervix.

"The left tube and ovary were of about normal size and appearance, externally and on section.

"The right ovary was replaced by a cystic mass, 8 cm. in diameter. The peritoneal surface was pale and smooth. The tube was stretched across the surface of the cyst and was adherent to it. The cyst was unilocular and was filled with clear, straw-colored fluid. The wall measured about 2 to 4 mm. in thickness. The lining was pale and smooth.

"*Provisional Diagnosis.*—Epidermoid carcinoma cervix uteri. Unilocular, simple serous cystadenoma ovary, right. Normal tube bilateral. Normal ovary, left.

"*Sections.*—The section of right ovarian cyst showed an outer zone of normal ovarian stroma. Scattered through this were several small cysts lined with granulosa cells. The lining of the cyst was made up of pink-staining fibrous tissue and a broken layer of low cuboidal epithelium.

"The tube showed normal folds of mucosa with no inflammatory infiltration.

"*Diagnosis.*—Epidermoid carcinoma cervix uteri (gross). Normal tube, right. Simple serous cystoma ovary, right, benign. Normal tube and ovary, left (gross). (Note by Dr. Hugh Warren.)

"This was one of the few cases in which we had no microscopic examination. The specimen was such a beautiful one that it was preserved intact for museum purposes. There was no doubt of the character of the growth, as shown by its speedy return.

"In December, 1930, the patient began to have a watery discharge which continued and became very fetid. She had been running a temperature of 99.2° F. and sometimes 100° F., in the evenings.

"When I saw her on March 10, 1931, the vaginal vault was filled with a new growth, fully 8 cm. in diameter. There was also a small, friable growth in the right vaginal vault.

"The patient was referred to Dr. Curtis F. Burnam for irradiation."

We extracted the following from Dr. Burnam's communication:

"My first treatment was on March 11, 1931, when I introduced eighteen removable gold tubes into the growth, and gave a total dosage of 2.495 Gm. hours. On March 15, 1931, I used four removable tubes, which were left in for two hours; the total dose on that date was 0.7536 Gm. hours, or 753.6 mg. hours. On April 8, I used a plaque in the vault of the vagina, containing 1694 mc., for eighteen minutes. This amounted to a gram half hour.

"On April 9, 10, and 11, the patient was given x-ray treatment. The factors used were a distance of 57 cm., 1 mm. aluminum plus 1 mm. copper and several millimeters of sponge rubber, and I used a technique which I have rarely indulged in since. On April 9, I gave 800 roentgens over the abdomen, through a single portal, 7 by 7 cm. On the tenth, new areas of skin were taken and a similar dosage given to two areas. On April 11, two posterior portals were used with the same dosage. The total amount was 4,800 roentgens on the skin.

"In addition, on April 11, I gave 1 Gm. half hour of radium by a permanent implant into the left parametrium. On May 6 and 7, x-ray was again given.

"The patient cleared up very nicely. So far as I could make out, the local growth disappeared completely."

There never were any symptoms or signs of bowel irritability nor postirradiation proctitis.

She remained well in the interval of eight and one-half years until about the first of December, 1939, when she became unusually constipated. Laxatives provoked a diarrhea and abdominal cramps. These symptoms subsided in a few days and were succeeded by vague abdominal discomfort with distention but without vomiting. On Dec. 13, 1939, the patient was awakened by a sharp pain in the right upper abdominal quadrant. This was followed by the passage of a large amount of bright red blood from the rectum. The bleeding continued at such an alarming rate that she was admitted to The Western Pennsylvania Hospital the same day.

Upon admission the patient was a normal, obese, white woman except for a slightly distended abdomen and hyperactive peristalsis. Laboratory findings were not abnormal. She was given fluids parenterally, later by mouth, and oil retention enemas. Within forty-eight hours the bowels moved, and there was no further bleeding.

A roentgenogram of the colon showed a point of obstruction at the junction of the descending colon and sigmoid (Fig. 1, *B*). There was distention of the sigmoid and rectum, but no barium passed beyond the narrowing. There was no channel typical of a new growth and the obstruction was interpreted as an inflammatory stricture due to surrounding adhesions. A metallic foreign body resembling a radon seed was adjacent to the obstruction (Fig. 1, *A*).

Sigmoidoscopic examination was unsuccessful in reaching the lesion. Laparotomy was advised but the patient refused it. She left the hospital only to return within a month because of the recurrence of abdominal pain.

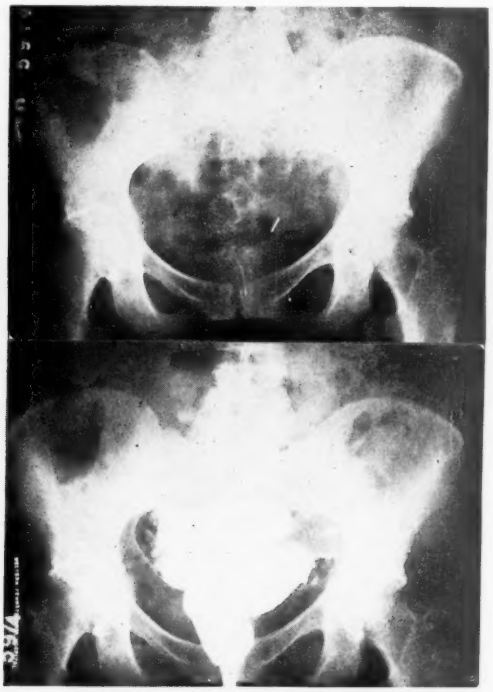


Fig. 1.—*A*, Roentgenogram of the pelvis with a metallic foreign body resembling a radon seed opposite the left ischial spine. *B*, Colon examination showing obstruction to the passage of barium at the junction of the descending and sigmoid areas.

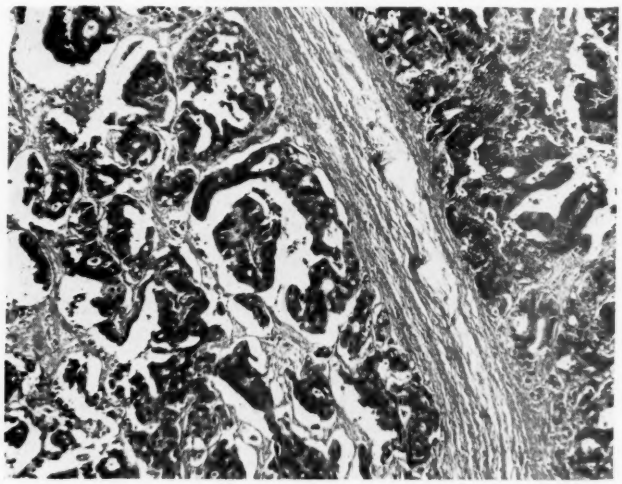


Fig. 2.—Typical adenocarcinoma of the colon discovered nine and one-half years after a primary malignant tumor of the uterine cervix.

On Jan. 29, 1940, with the patient under ether anesthesia, an exploration was made which disclosed the sigmoid and rectum densely adherent to the surrounding structures. A hard mass approximately 6 cm. in length was present about the

junction of the descending colon and the sigmoid. With difficulty the sigmoid was separated and resection of a typical carcinomatous mass accomplished. Two centimeters distal to the neoplasm, a benign stricture about 1 cm. in diameter was present. This was not apparent until the intestine was opened. It seemed to involve only the mucosal and muscular layers with a bandlike annular constriction. Anterior to this was found a radon seed which was the foreign body seen in the roentgenogram. There was no evidence of neoplasm in the pelvic organs nor metastases in abdominal lymph glands or liver. It was impossible to remove the stricture because sufficient bowel could not be freed.

The pathologic specimen consisted of large bowel 6 cm. long. The major portion of it was occupied by a firm mass with a craterlike ulcerated depression from the mucosal surface 3½ cm. in diameter and 1½ cm. in thickness. The serosal fat was hemorrhagic. Longitudinal section through the specimen exhibited infiltrating, grayish white, translucent tissue. The microscopic diagnosis was "adenocarcinoma, poorly differentiated with tumor extending to subserosal fat" (Fig. 2).

A smooth postoperative course was interrupted by a urinary tract infection, phlebitis of the right leg, and a partial disruption of the wound due to severe coughing. She was discharged two and one-half months following operation, and at the present time (July 1, 1940), six months after operation, she has gained in weight and is having no symptoms.

COMMENT

In a fairly extensive search of the literature we could not find a similar case. The benign stricture was typical of those due to irradiation and was probably the result of a combination of radium and roentgen therapy, although the amount certainly was not excessive. There had been no immediate intestinal reaction following irradiation and the stricture was not clinically significant until she developed signs and symptoms of colonic malignancy. Although bleeding from telangiectases has been reported[3] as the chief complaint in some cases of stricture, a nine-year interval without bleeding made this possibility less likely and suggested new growth rather than stricture. The rarity of finding a benign stricture and a malignant growth simultaneously precluded the possibility of diagnosing both conditions before operation.

The attack of amebic dysentery suffered twenty-two years previously plus the radical panhysterectomy might have been contributing factors in the development of the benign stricture, in that adhesions held the bowel fixed in one position so that it received a maximum exposure of irradiation. The possibility of amebic dysentery producing an isolated stricture was considered remote. Multiple healed ulcers rather than stricture would have been expected. The carcinomatous area was situated directly above the stricture so that stasis might also have been one of the local inciting factors for the development of the neoplastic change in a cancer-susceptible individual.

In our opinion, the carcinoma of the bowel was a second primary tumor. The chance of this being a late metastasis is unlikely because of the typical microscopic appearance of adenocarcinoma of the colon without evidence of invasion from the outside. The recurrent malignant primary tumor of the uterine cervix for which the patient was treated nine years ago remains cured, according to our present standards for the evaluation of such data.

SUMMARY

Both a benign postirradiation stricture and primary adenocarcinoma of the proximal sigmoid colon were found nine years following successful radiation therapy for a recurrent malignant lesion of the uterine cervix.

REFERENCES

(1) *Collins, E. N., and Jones, T. E.:* Surg. Gynec. Obst. **59**: 644, 1934. (2) *Corscaden, J. A., Kasabach, H. H., and Lenz, M.:* Am. J. Roentgenol. **39**: 871, 1938. (3) *Jones, T. E.:* J. A. M. A. **103**: 1678, 1934.

4800 Friendship Avenue

FIBROMYOMA OF UTERINE CERVIX, PEDUNCULATED AND EXPELLED FROM VAGINA

RICHARD TORPIN, M.D., AND B. C. BEARD, M.D., AUGUSTA, GA.
(From the Department of Obstetrics and Gynecology, University of Georgia School of Medicine)

E. S., negress, aged 29 years, slender constitutional type, poorly nourished, entered the hospital complaining of pain due to a grapefruit-size mass hanging from her vagina. She stated that thirty hours previously she was sitting on a slop jar and had two or three hard pains, rather like labor pains, and felt something slip down between her legs. She tried to push it back, but was not successful (Fig. 1). She had been sick for about three weeks in and out of bed suffering with pelvic pain, some nausea and vomiting, and a profuse vaginal discharge. A midwife treated her with tablets and douches. She states that she had noticed a "knot" in her lower abdomen for three or four months; and for the past three months had not been able to have sexual intercourse because of a mass filling her vagina.

For three or four months her bowel movements have been regular, but when she urinated only a small amount of urine was expelled, leaving a feeling of more in her bladder; but after the tumor was expelled and later excised, her urine flowed freely. Her last menstrual period was a few days late but of normal duration and flow. Previous periods were normal. She gave a history of first menstruating at twelve or thirteen years of age, always regular and of five or six days' duration; moderate flow and there was no change even during the last few months. She married at the age of 13 or 14 and has one child 13 years old. She stated that she had had 3 miscarriages at two to four months each, the last one being about one year ago.

The physical examination revealed otherwise essentially normal findings in a malnourished negress with subnormal mentality; temperature 100° F.; pulse, 110; respiration, 20. Her blood pressure was 130/70; her red blood cell count 4,000,000; hemoglobin 10 Gm. per 100 c.c.; white cell count 16,000 with 50 per cent polymorphonuclear leucocytes and 50 per cent lymphocytes. The urine had a small amount of albumin, but a clean specimen was difficult to obtain because of the mass protruding from her vagina.

The operation was performed with the patient anesthetized by cyclopropane inhalation. Because of a rather small pedicle the size of a large thumb attached to the lower edge of the posterior wall of the cervix, the diagnosis of a tumor rather than an inverted uterus was evident. The cervical canal, which was anterior to the pedicle, was dilated enough to admit a small finger, and when the protruding mass was pulled down, the cervix appeared at the introitus. The fundus uteri was enlarged and boggy, the size of a lemon, and it was freely movable and there were no lateral masses. The cervix was not elongated; thus the expulsion of the tumor from the vagina prolapsed the cervix and fundus to the introitus. Previously the uterus most certainly must have been elevated in the abdominal cavity nearly to the umbilicus. The pedicle was clamped and the mass excised. The clamp was then replaced by hemostatic ligatures. She made a rapid recovery without appreciable elevation in body temperature.

The gross pathology consisted of a fetal head-sized mass somewhat encapsulated but with a surface slightly irregular and necrotic in places. The consistency was homogeneous and indefinitely cystic feeling.

The mass measured 15 by 12 by 8 cm. and weighed 745 Gm. The cut surface was that of an edematous fibromyoma with a few small irregular cystic areas filled with serous transudate.

The pathologic report stated that "most of the surface is ulcerated and inflamed, but in a few areas it is covered by stratified mucous epithelium. At one end there is a raw area 4 cm. in diameter."

Fibromas or fibromyomas of the uterine cervix obviously may be classified into several types: (a) those that arise in the upper part of the cervix and grow upward into the abdominal cavity, elevating the fundus above it; (b) those that arise in the middle portion of the cervix and extend out into the interstitial tissues of the lower broad ligaments laterally; under the urinary bladder anteriorly, or into the tissue between the peritoneum and vaginal mucosa posteriorly; (c) those that grow from the vaginal portion of the cervix and spend their entire existence within the vaginal cavity or protruding from it; (d) those that arise in the cervical stump remaining after supracervical hysterectomy operation.

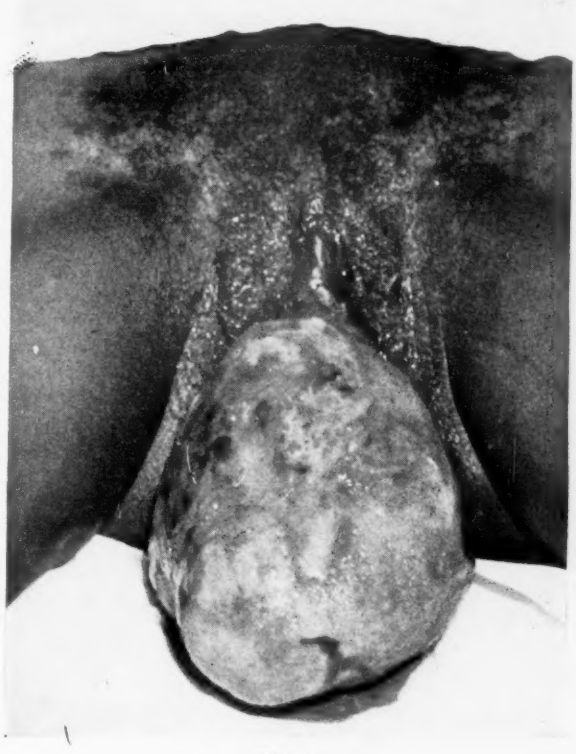


Fig. 1.

According to Counseller and Collins, Turunen in 1930 adequately reviewed the literature and collected 112 cases of cervical fibroma or fibromyoma and that 40 of these were encountered in pregnancy when the tumor either blocked or rendered childbirth exceedingly difficult. We find that there have been records of a dozen or more since that time. It might be of interest to review all cases and place them in the above classification. However that has not been done but some of the recent instances may be so presented.

Type A tumor arising from the upper portion of cervix elevating the fundus above it, is illustrated by Greenhill's first and third cases and by Counseller and Collins' case and by Reel's case. These four instances, apparently all in white women, aged 42, 34, 49, and 25 years, respectively, had tumors in the lower part of the abdominal cavity and in the pelvis elevating the fundus in each case to or above the umbilicus. These tumors were all large, weighing 4 pounds each,

or more; and in the ones of Counseller, Collins and Reel extended downward into the vagina through a well dilated cervical canal. In Reel's case the tumor in a white girl, 25 years old, weighed 7 kg.

Type B, interstitially growing tumor, is illustrated by Hall's case in which the tumor presented at the vulva, separating the labia more than two inches. The patient was a white woman 44 years old, the mother of 9 children, the youngest 11 years old. She had symptoms of pelvic distress, hypermenorrhea, and an acute attack of urinary retention. This tumor, probably as large as an orange, apparently arose from the posterior wall of the cervix and dissected interstitially between the posterior vaginal wall and the rectum and presented at the introitus of the vagina. It was quite bloodlessly enucleated through an incision in the vaginal wall covering it.

Type C, pedunculated cervical tumor within or protruding from the vagina, is well illustrated by the cases of Counseller, Cox, Church and Paterson, Christopher, von Zur-Mühlen and ours. All of these reports are accompanied by illustrations and each tumor developed entirely intravaginally and was pedunculated to the cervix. The patients, apparently all Caucasian, except ours, were aged 46, 37, 48, and 29. In general the effect on the uterine bleeding at menstruation was not marked in this class, but there was more or less urinary disturbance and in two cases the tumor specifically interfered with sexual intercourse. In two of the cases the tumor body was expelled from the vagina. In three of the cases the tumors were attached to the posterior lip of the cervix and in the other to the right lateral wall. One had operative treatment by abdominal total hysterectomy, the other three by vaginal extirpation of the tumor. All recovered. The pictures illustrating Christopher's, von Zur-Mühlen's, and our cases could be substituted for one another without loss of accuracy.

Type D, arising from a remnant of cervix, is illustrated by cases reported by Fletcher, Moench and Greenhill's second case. All of these apparently were in white women, aged 35, 42, and 43, and the time interval between operation of supracervical hysterectomy and the treatment of the tumor in the cervical stump was eight years, one year or so, and seventeen years. The weights of these tumors were 12½ pounds, 660 Gm., and about 2 pounds, respectively.

REFERENCES

(1) *Caruso, P.:* Am. J. Obst. & Gynec. **33:** 696, 1937. (2) *Greenhill, J. P.:* Ibid. **31:** 678, 1936. (3) *Counseller, V. S., and Collins, D. C.:* Ibid. **30:** 108, 1935. (4) *Fletcher, H. N.:* Brit. M. J. **1:** 300, 1935. (5) *Cattell, R. B.:* S. Clin. North America **13:** 707, 1933. (6) *Counseller, V. S., Cox, F. W., Church, G. T., and Paterson, S. J.:* Ibid. **13:** 966, 1933. (7) *Reel, P. J.:* Am. J. Obst. & Gynec. **14:** 386, 1927. (8) *Moench, L. M.:* M. Clin. North America **12:** 1584, 1929. (9) *Christopher, F.:* Am. J. Obst. & Gynec. **11:** 668, 1926. (10) *Greenhill, J. P.:* Ibid. **19:** 860, 1930. (11) *von Zur-Mühlen, F.:* Zentralbl. f. Gynäk. **51:** 2483, 1927

Todd, T. F.: Relief of Intractable Pain in Carcinoma of the Cervix Uteri, Lancet **2:** 1305, 1939.

The author reports upon the relief of intractable pain in 84 cases of cervical carcinoma, 3 cases of rectal carcinoma, and 1 of prostatic carcinoma. These are subdivided in 2 types: visceral pain in 42 and somatic pain in 46 cases. Intractability can only be determined after a period of hospital observation and such an assay of the amount of pain should be made before operative relief is attempted. In visceral pain presacral neurectomy gave relief in all but one case. In somatic pain the author recommends intrathecal injection of absolute alcohol. There were four failures in this group. In addition to correct positioning of the patient, the most important points in the alcohol injection are to inject no faster than 0.5 c.c. in two minutes and not to inject more than 1 c.c. on any one occasion.

Carl P. Huber.

CHORIOANGIOMA OF THE PLACENTA

JOHN H. FISHER, M.D., M.Sc., LONDON, ONT., CANADA

(From the Department of Pathology and Bacteriology, University of Western Ontario Medical School)

CHORIOANGIOMA of the placenta is a benign tumor arising from chorionic mesenchyme and appears to be comparatively rare. Most of the papers on the subject contain reports of only single cases. It is barely mentioned in most of the accepted textbooks on obstetrics and gynecology, in part no doubt, because it seems to be of little definite clinical significance but perhaps because it has been largely overlooked.

Marchetti, in a very comprehensive article, has completely reviewed the literature up to 1939 in which he found 209 apparently authentic cases of chorioangioma of the placenta and added 8 cases of his own. However, it appears that he has overlooked a case reported by Rhamy. Subsequent to Marchetti's article a paper by Kotz and Kaufman and one by Siegel and Holley have appeared in the American literature, each recording a case of chorioangioma of the placenta. Kotz and Kaufman have reviewed the literature between 1924 and 1938 and pointed out that only 46 cases have been reported in that fourteen-year period.

The object of this paper is to record briefly two additional cases of chorioangioma of the placenta, including the gross and microscopic features of the placental tumors.

CASE REPORTS

CASE 1.—Mrs. T., white, gravida iv, aged 28 years, had had 3 normal pregnancies previously and the three children are living and well. The antenatal course in this fourth pregnancy was uneventful, although she admitted having attempted to produce an abortion by inserting some sort of wire stilette into her cervix which produced a little vaginal bleeding. No untoward effects developed and the pregnancy progressed. A normal full-term infant was delivered spontaneously by breech presentation on Feb. 2, 1939. There was no hydramnios and no excessive blood loss. The mother's blood serum was negative for syphilis. Before the placenta was expressed intact by the Credé technique, it was noticed that the uterus was unusually large and presented a peculiar heart-shaped form, so much so that the possibility of a twin pregnancy was suggested. The puerperium was essentially normal, although at one time it appeared that she was developing a femoral phlebitis. The attending physician sent the placenta to me for examination because of its peculiar shape and the presence of a large tumor-like mass distorting the amniotic surface.

Description of Placenta and Tumor.—The placenta was discoid in shape, weighed 1,150 Gm., and measured 17 cm. in its greatest diameter. The umbilical cord was eccentrically attached, lying at the margin of the tumor. The maternal surface was intact and free from gross changes except for three small infarcts. The fetal surface presented a large, lobulated tumor mass, measuring 14 by 11 by 7.5 cm. and protruding 5.5 cm. above the general fetal surface. The tumor was dusky, purplish red in color, semifluctuant in consistency and covered with smooth, intact but greatly stretched and elevated amnion. On cross section of the tumor in a vertical plane at right angles to the fetal surface of the placenta, the cut surface showed a rather variegated structure, partly solid and partly spongy and cystic. The compact gray areas appeared fibrous in structure, the spongy areas proved to be angiomatous in nature and the pseudocysts were filled with dark blood. The tumor was obviously arising from chorionic tissue from which it was quite well demarcated. The main gross features of the tumor are shown in Figs. 1 and 2.

Several blocks of tissue were selected for microscopic study from representative areas, four of which are outlined in Fig. 2. Area 1 included the junction of the tumor and placenta (Fig. 3). Area 2 was angiomatous in structure (Fig. 4) while

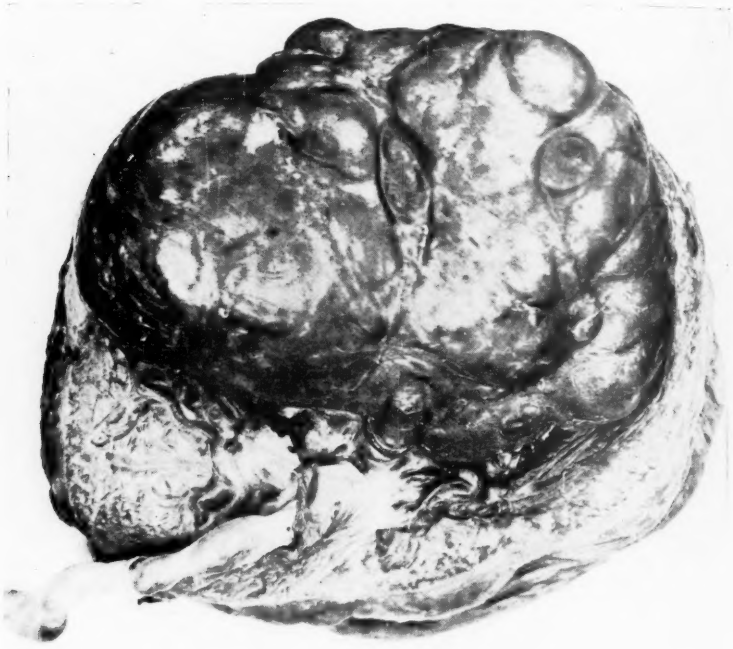


Fig. 1.—Case 1. Placenta and tumor viewed from the fetal surface. Note the large, lobulated, protruding tumor mass.

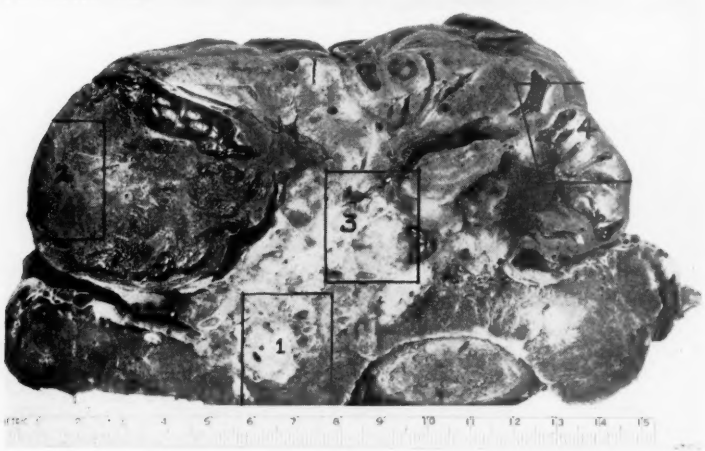


Fig. 2.—Case 1. Cut surface of vertical section through tumor and placenta at right angles to fetal surface, showing compact fibrous areas, spongy angiomatous areas, and several "blood cysts." Sections were taken from the outlined areas.

Area 3 was chiefly fibrous in character. Area 4 presented a combined fibrous and angiomatous composition containing several endothelial-lined "blood cysts." The angiomatous areas consisted of countless endothelial-lined spaces, dilated, and

filled with blood. These capillary blood channels were separated by thin strands of dark-staining fibroblasts (Fig. 4). Some of the fibrous areas were composed of compactly arranged, adult collagenous fibers, while in others the structure resembled loosely arranged, embryonal mesenchymal cells, producing a myxomatous-like tissue. In these latter areas and also in the stroma of the angiomatous areas,

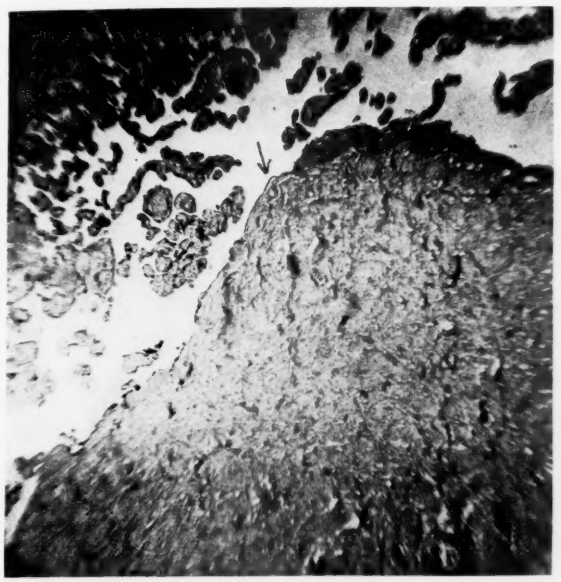


Fig. 3.—Case 1. Photomicrograph of junction between tumor and placenta. Area 1 outlined in Fig. 2. A single layer of syncytium (arrow) covers the tumor. ×36.

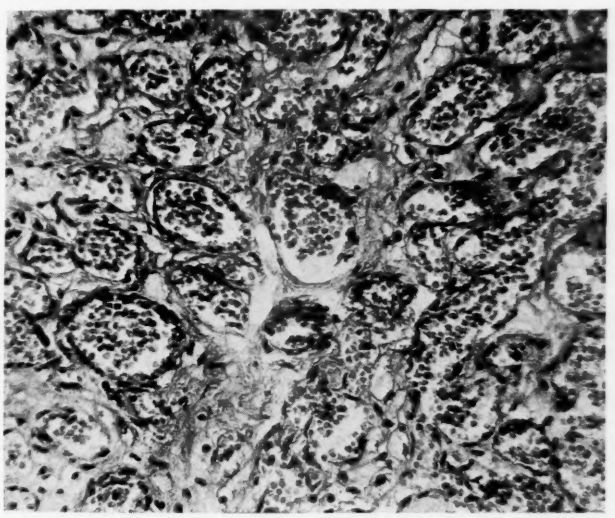


Fig. 4.—Case 1. Photomicrograph of Area 2, Fig. 2, showing angiomatous structure of tumor. ×230.

there were found quite numerous, rather large mononuclear cells with fairly abundant, acidophilic cytoplasm, perhaps some sort of primitive blood cell. Incidentally, no erythroblasts or other evidence of erythroblastosis were detected in the chorionic villi. The "blood cysts" were lined with endothelium which, at

some points, was heaped up into little syncytial masses. The cystlike spaces contained blood, and occasional focal calcareous deposits were present in the walls of the cysts. Sections of the placenta proper did not appear abnormal.

CASE 2.—Mrs. P. M., white, gravida i, aged 21 years. The last menstrual period was on July 10, 1936, the expected date of confinement April 17, 1937. The antenatal course was normal up to the sixth month, at which time the blood pressure was slightly raised to 142/94. At the seventh month the blood pressure was 158/104, the urine contained albumin 2+, and hydramnios was noted. At seven and one-half months the blood pressure was 164/116. X-ray picture showed an abnormal fetus and medical induction was employed. The membranes were

Fig. 5.—Case 2. Placenta and multiple chorioangiomas viewed from the maternal surface. Twenty or more pedunculated tumors of various sizes are attached to the chorionic villi.

artificially ruptured and delivery was spontaneous and easy. The infant was an approximately seven and one-half months stillborn, female, anencephalic monster with complete spina bifida. The placenta was delivered intact by the Credé technique. Blood loss was slight and the puerperium was normal. This patient subsequently delivered a normal, full-term infant in another city about Aug. 1, 1938, after a normal antenatal course.

Placenta.—The placenta was of normal size, measuring 17 by 16 by 3.5 cm. Its fetal surface showed nothing unusual. The umbilical cord was attached eccentrically. The maternal surface presented 25 pedunculated tumors attached to the chorionic villi by delicate, vascular stalks. The tumors were slightly mottled, reddish gray in color and varied in size from a walnut (3 by 2.5 by 2.5 cm.) to a millet seed (1 to 2 mm.). They hung down from the maternal surface attached by delicate stalks much like small red tubers or potatoes. Some of them lay partially or completely buried between cotyledons or villi. They were most numerous in the central part of the maternal surface. About 20 of the tumors may be seen in Fig. 5. Their cut surface presented a color and consistence like kidney tissue. Otherwise, the placenta showed nothing remarkable.

Microscopic study showed that the tumors were partly covered with a membranelike layer of trophoblastic epithelium. They presented an angiomatous structure corresponding to the vascular or mature type of chorioangioma as described by Marchetti. They were composed of abundant blood vessels, chiefly of capillary caliber, closely packed together with little supporting stroma (Fig. 6). In some areas the fibrous connective tissue was more abundant but loosely arranged and rather immature-appearing. A small amount of old blood pigment was present in the stroma both lying free and contained within large phagocytic cells. Sections of the placenta itself appeared essentially normal.

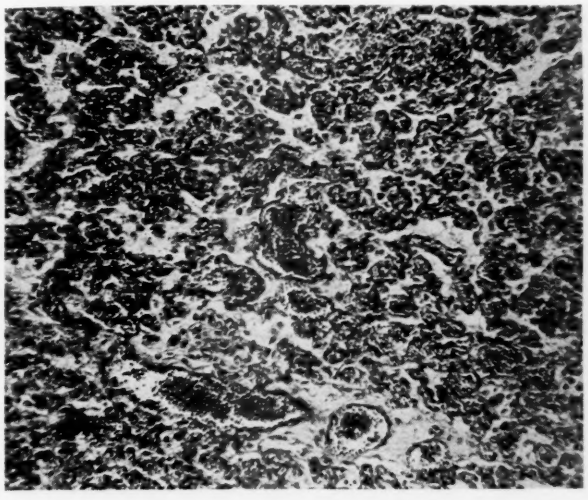


Fig. 6.—Case 2. A typical angiomatous area. ×100.

COMMENT

In both cases here reported, the chorioangiomas show some unusual features. In Case 1, the tumor was exceptionally large. Few larger ones have been reported. The placenta as a whole, including the tumor, was approximately 550 to 600 Gm. above normal weight. The tumor was situated in the more common location, on the fetal surface. The question was raised in Case 1 as to whether or not the patient's attempt to produce an abortion might have acted as an etiologic factor in the production of the tumor, but this seems highly improbable. Syphilis, mentioned by some writers as an etiologic factor, exerted no influence in these two cases.

Case 2 is unusual in that the tumors were multiple and numerous. In most instances, the tumor is single, although the number in any one placenta may be as high as 100. The tumors were attached to the maternal surface of the placenta in Case 2. While this is a less common location than the fetal surface, it is not particularly uncommon.

Opinions differ widely concerning the clinical significance of chorioangioma of the placenta. Kotz and Kaufman state that, in their opinion, there is a definite correlation between chorioangioma and hydramnios, premature labor, stillbirth, and post-partum hemorrhage. Marchetti, on the other hand, feels that, with possible rare exceptions, chorioangioma possesses no clinical significance. Analyzing the 2 cases which I am reporting, it is found that hydramnios was present in Case 2 but not in Case 1. Premature labor occurred in Case 2, but it was artificially induced, while in Case 1 the pregnancy went to term and labor onset was spontaneous. Case 1 produced a normal, living, full-term infant, while the infant in Case 2 was a stillborn, anencephalic monster with spina bifida. No post-partum hemorrhage was encountered in either case. The attending physician in

Case 1 was inclined to think that the large placental tumor accounted for the breech presentation, but it is more likely that the association was merely coincidental.

SUMMARY

1. Two cases of chorioangioma of the placenta are reported, including the gross and microscopic features of the tumors.

2. In one case the tumor was solitary but exceptionally large. In the other case the tumors were multiple and pedunculated.

3. In one case there was an associated hydramnios and a stillborn abnormal infant.

4. Retained placenta and post-partum hemorrhage were not encountered in either case.

5. A diligent search for chorioangioma of the placenta would probably show a higher incidence of this tumor than at present reported, as undoubtedly some instances have been overlooked in the past.

The author is greatly indebted to Dr. J. L. Duffy for the clinical notes and for permission to publish Case 1 and to Dr. Evan Shute for Case 2.

REFERENCES

(1) *Kotz, Jacob, and Kaufman, Morton S.:* M. Ann. Dist. Columbia **8:** 106, 1939. (2) *Marchetti, Andrew A.:* Surg. Gynec. Obst. **68:** 733, 1939. (3) *Rhamy, B. W.:* J. Lab. & Clin. Med. **22:** 899, 1937. (4) *Siegel, Louis A., and Holley, Emerson:* Am. J. Obst. & Gynec. **38:** 353, 1939.

PRIMARY DIFFUSE ADENOCARCINOMA OF THE VAGINA*

Monte C. Piper, M.D., Rochester, Minn.

(From the Section on Obstetrics and Gynecology, the Mayo Clinic)

TWO cases of primary diffuse adenocarcinoma of the vagina have been observed in the Mayo Clinic within two years. The first case was reported by Scannell in 1939, who credited Broders with the tissue diagnosis. The second case is reported herewith and some features which were observed in both cases of this apparently rare condition will be mentioned.

An instance of diffuse adenosis of the vagina was reported by Bonney and Glendining in 1911, and they referred to a report of a similar condition by Prueschen in 1877. In neither of those cases had malignant change taken place but active glands secreting mucinous fluid were present.

REPORT OF CASE

In February, 1940, a white woman, aged 29 years, consulted the gynecologic department because of menstrual irregularity, intermenstrual pelvic pain of two and one-half years' duration and intermenstrual spotting. The patient had had scarlatina at the age of 5 years, had undergone appendectomy when she was 17 years of age, had "dry pleurisy" at the age of 18 years, and had been subjected to tonsillectomy at 20 years of age. Two anal operations had been performed, one at the age of 27 and the other at the age of 28 years.

The dermatologic history was interesting. Lichen planus had appeared about the ankles at the age of 21 years and eventually had involved most of the bodily surfaces except the face. Specimens of skin taken from the back for biopsy had confirmed the diagnosis. At the age of 22 years, in 1932, when the patient first had visited the clinic because of the cutaneous condition, the lesions had involved

*Presented at a meeting of the North Dakota State Society of Obstetrics and Gynecology, Minot, N. D., May 7, 1940.

Submitted for publication July 18, 1940.

the external genitalia and had been described as purplish, flat, shiny, angular areas scattered all over the genitalia. Also, at this time there were lesions in the mouth consisting of firm, whitish material about the dentate margins; a biopsy of the mucous membrane revealed filaments resembling mycelia, suggestive of thrush. However, a positive culture of significant fungi was not obtained. When the patient was 25 years of age, a dermatologist had recorded that the mucous membrane of the vagina resembled that of the mouth but the Wickham's stria seen in cases of lichen planus were absent. Also when the woman was 25 years of age, it was noted that an associated seborrheic dermatitis had resulted in areas of "alopecia cicatrisata" to which phenol had been applied. The conjunctivae of both eyes had been the site of superficial punctate keratitis, with small lesions near the limbus resembling subepithelial cysts. Various therapeutic agents had been employed; these had included, at first, ultraviolet light and subsequently mercury pills; Fowler's solution by mouth, sodium cacodylate hypodermically; local applications of formalin, acriflavine, and gentian violet solution; metaphen ointment to the conjunctivae, and a variety of vitamins. The condition of the mouth was somewhat alleviated following administration of the vitamins.

The metabolic history also was of interest. In 1934, the metabolic rates had been -3 and -5 per cent; this was at a time when the patient was taking estrogenic substance because of a menstrual irregularity, as will appear. Early in 1938, she said, readings of the metabolic rates had been -21 and -23 per cent. The history was somewhat suggestive of myxedema. Thereafter, for about a year, the woman had taken desiccated thyroid gland daily. For the year before her admission in 1940 she had continued to take desiccated thyroid gland but in a larger dose than before, namely, in doses of 3 gr. (0.2 Gm.) per day. This dose apparently lessened her fatigue and her tendency to gain weight. On admission, her metabolic rate was +3 per cent.

Menstruation had begun at the age of 10 years and had occurred every twenty-eight days until the age of 22 years, or about a year following onset of the lichen planus. Then menstruation had begun to increase in frequency. At the age of 24 years intermenstrual spotting had begun and had continued for more than a year. This was thought to be on the basis of ovarian dysfunction. Rectal examination then had given negative results except that it had disclosed the presence of a congenital type of uterine retroversion and estrogen had been administered, apparently with some good effect on the spotting. At the age of 27 years, midmenstrual cramps had appeared on the left side; sometimes these were rather severe and were accompanied by bleeding during the intermenstrual interval. Menstruation had become irregular and dribbling of menstrual material had continued for eight days after a normal two days of flow. This condition had been gradually progressive up to February, 1940. Dilatation and curettage had been performed elsewhere in February, 1938, and in August, 1939, and following the last of these operations a tentative diagnosis of endometriosis had been made.

The patient's mother had died of endocarditis at the age of 42 years and one sister had lichen planus.

The woman had an erect, well-proportioned figure, somewhat broad shoulders, a strong waist, not particularly prominent hips or breasts but no abnormal hirsutism. Her height was 5 feet, 6½ inches (169 cm.), her weight was 150 pounds (68 kg.), and she seemed alert and intelligent. There was an area of alopecia over the vertex of the scalp. Buccal mucous membranes were of a velvety, bluish red, and the skin revealed some residual evidences of lichen planus. Sensitivity over both lower abdominal quadrants was increased.

The external genitalia were hypoplastic or atrophic and revealed several abnormal manifestations (Fig. 1, *A*). The fissure of the vestibule was partly sealed from both sides, and there was no apparent evidence of clitoris or prepuce. The labia minora were small, shortened, and flaccid, and the introitus was atrophied, small, and hypersensitive. The urethral meatus was a vertical slit seen only

when some projecting tissue on the right of the orifice was pushed farther to the right. This projecting tissue protruded 1 cm. and was attached to the right of the meatus by a parallel base, 1 cm. long and less than half that broad. This peculiar tissue seemed bluntly pointed at times and again slightly more lobulated, as though it were collapsed or less dense. It was suggestive of erectile tissue. There was no such formation on the left of the meatus. It did not appear to be an ordinary caruncle or as prolapsed urethral tissue. A serosanguineous fluid, slightly blood stained, exuded from the vagina, and the orifice was too sensitive to permit examination by more than one finger. The anterior vaginal wall was

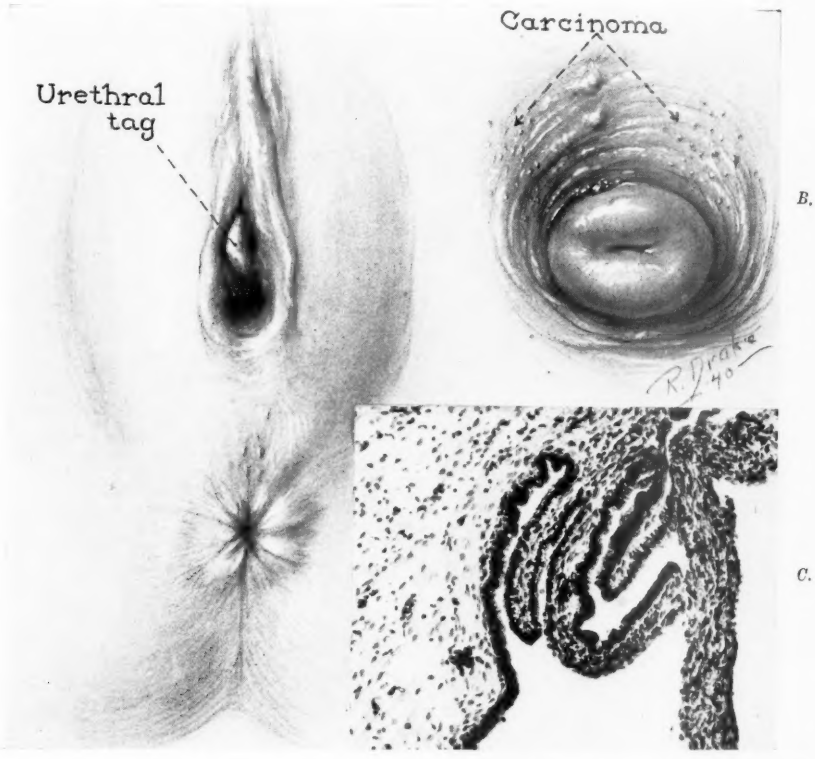


Fig. 1.—*A*, Abnormalities of external genitalia; *B*, nodular projections in anterior vaginal wall; *C*, papillary adenocarcinoma, Grade I.

short, the cervix was anterior and the medium-sized fundus had undergone retroversion, Grade 3. The adnexa seemed normal to palpation. The vaginal wall, each side of the vault and in the anterior cul-de-sac, felt strangely granular (Fig. 1, *B*). Along either side of the vaginal portion of the urethra was a fibrous strip in which were nodular projections that felt like small submucosal fibromas. They were rounded, firm, and smooth and the largest was about 3 mm. in diameter. One of these was on the left; three were in a row on the right and seemed to connect with the perimeatal projection mentioned before. With the aid of a local anesthetic and a small speculum, the vaginal walls were brought into view. In either lateral vault and over the portio vaginalis in the anterior cul-de-sac were fine, glistening projections, as though grains of sand were beneath the epithelium. Some refracted light as though they were small, mucinous cysts, and others were darker red than the color of the surrounding surface. Twelve of these were counted on the right and nearly as many on the left, while perhaps eight were seen over the portio vaginalis. The periurethral nodules in

the anterior vaginal wall had the more usual appearance of submucous fibromas. Several of the smaller projections from each lateral wall and over the cervix in the cul-de-sac were snipped out with a biopsy punch.

The pathologist reported papillary adenocarcinoma Grade 1 in all situations (Fig. 2). Subsequently specimens for biopsy were obtained from the projecting tissue at the side of the meatus as well as from the nodules to the right of the urethral tube, in the vagina. These were inflammatory tissue and when the slides were reviewed subsequently by the pathologist, the tissue was said to contain, in one area, a structure resembling the spaces observed in erectile type of tissue. A specimen from the endocervix proved to be only a blood clot. Surgical and radiologic consultation resulted in the administration of a total of 1,526 mg. hr. of radium given in four divided applications to the vaginal wall.

COMMENT

The unusual features of this case were the chronic ectodermal lesions and the abnormal basal metabolic variations. Whether the periurethral tissue may be an evidence of bisexualism is considered a possibility.

Features common to this case and to the case reported by Scannell are that the patients were approximately of the same age; the duration of symptoms was nearly the same; there were slight evidences of masculinity in bodily contour; the dermal structures were sensitive to mild irritation; there was a history of vaginal irritation of long duration, and adenocarcinomatous tissue of low grade of malignancy was diffusely spaced in the vaginal epithelium.

REFERENCES

(1) *Bonney, Victor, and Glendining, Bryden:* Proc. Roy. Soc. Med. **4**: 18, 1911. (2) *von Preuschen:* Quoted by Bonney, Victor and Glendining, Bryden. (3) *Scannell, R. C.:* Am. J. Obst. & Gynec. **38**: 331, 1939.

LIPOMA OF THE UTERUS

Fred L. Ritter, M.D., and Sydney W. Stringer, M.D.,
Syracuse, N. Y.
(From the Department of Gynecology, Syracuse University)

Lipoma of the uterus is a rare neoplasm. In 1922, Petersen[1] reviewed the literature on mixed tumors and collected 31 cases. Of this group, only 10 were classified as simple lipomas. Of the remaining 21 cases, 14 were called fibromyolipomas, 5 as lipomatous areas in mixed tumors, and 2 as liposarcoma. Twenty-eight per cent of the mixed tumors reported were considered to be malignant, in that metastases were reported. He added one case in which 94 per cent of the tumor consisted of fatty areolar tissue. Thirteen additional cases have since been reported, one each, by Preissecker,[2] Starry,[3] Dworzak,[4] Bride,[5] Engelhard,[6] Lund,[7] Muschik,[8] Nordin,[9] Burger,[10] Glas,[11] Humphrey and Mustard,[12] and two by Thaler.[13] One case, Humphrey and Mustard's,[12] was associated with carcinoma of the uterus, and one case, Engelhard,[6] was reported as a malignant lipoma. In view of the rarity of these tumors, it seems worth while to report another case.

CASE REPORT

Mrs. E. D., aged 57 years, had had a yellowish, watery vaginal discharge, occasionally slightly tinged with blood, for six weeks, slight backache, and a bearing down sensation. Menses began at 12. She had had two normal pregnancies; menopause at 45, with very little discomfort. She had no symptoms referable to the pelvis until the onset of the present trouble. Her general health had always been excellent. There had been no loss of weight and no gastrointestinal or urinary tract disturbance.

Physical examination was negative except for the pelvic findings. The uterus was enlarged, reaching 5 cm. above the symphysis, irregular in outline. A circumscribed nodular mass could be felt in the anterior uterine wall. Mobility was not diminished. There was no tenderness in the adnexal regions and no other masses could be felt.

Laboratory Data.—Red blood count 4,900,000. Hemoglobin 14 Gm. Red blood cells appeared normal. White count 7,600. Differential: polymorphonuclear leucocytes 71, lymphocytes 29. Sedimentation rate at the end of one hour 6 mm.

After a preliminary diagnostic curettage, a supravaginal hysterectomy was performed.

Pathologic Report.—The specimen consisted of a uterus, both tubes, and the left ovary. The tubes revealed some thickening at the fundal end and on section the wall was thickened and fibrosed. The ovary presented no abnormalities. The uterus measured 10 by 7 by 6 cm. and, bulging in the anterior wall, there was a

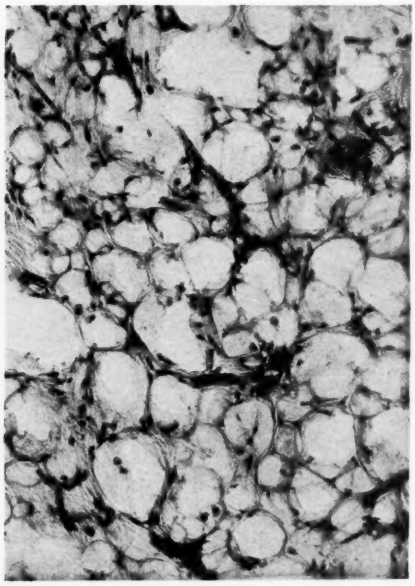


Fig. 1.—Hematoxylin-eosin stain. ×150.

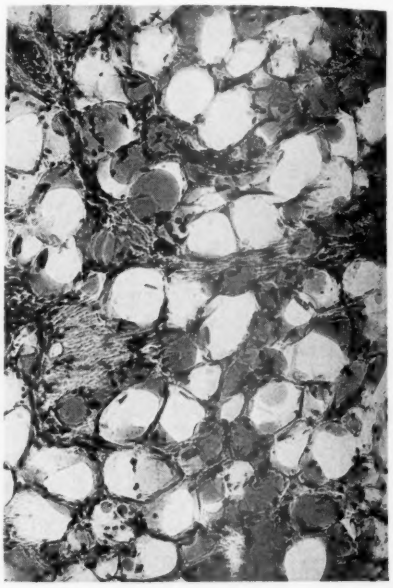


Fig. 2.—Scharlach R stain. ×150.

discrete, circumscribed mass 7 cm. in diameter, which had a definite capsule of uterine tissue about it. The mass was lemon yellow in color and rubbery in consistency. On section the color was uniform throughout, making the tumor stand out from the surrounding normal uterine tissue. The cut surface had the same appearance throughout. No macroscopic blood vessels were visible. The tumor mass could easily be peeled from the adjacent tissue.

Two centimeters from the large tumor, toward the fundus, was a second mass 3 cm. in diameter. This was similarly discrete and encapsulated, but was pearly white throughout and contained no yellow areas. This latter mass had the characteristic whorl-like appearance of leiomyoma of the uterus. The cavity of the uterus was distorted by the large mass and the endometrium was 1 mm. thick.

Microscopic Examination.—The histologic picture of sections stained with hematoxylin-eosin (Fig. 1) revealed a uniform structure composed of large cells with the nucleus pushed toward the periphery. These cells apparently contained no protoplasmic material and were supported by a very thin connective tissue stroma. Nowhere in the sections were there any leiomyomatous elements. Sudan III and Scharlach R (Fig. 2) stains revealed that the vacuolated cells were artefacts due to fixation and the cells were distended with fat. An osmic acid preparation

revealed a slight, if any, staining of the fat granules. One section revealed that the capsule of the tumor was connective tissue from which there extended delicate strands making up the stroma of the mass.

A section through the smaller tumor revealed no fat cells and the typical structure of a leiomyoma of the uterus. The endometrium was proliferative in type with some evidence of cystic change.

DISCUSSION

The histogenesis of fatty tumors of the uterus has not, as yet, received definite interpretation. Von Franque[14] views it as an example of metaplasia. Merkel[15] believes they arise from displaced embryonic mesoderm. Knox[16] considers them as supporting Conheim's theory of embryonic rests, which in developing, produce fatty tumors. Brunings'[17] belief coincides with that of Lockyer[18] who expounds the premise that lipomas of the uterus are the result of the transformation of muscle bundles into fat. In addition, the Wolffian duct theory of Wilms and the growth of true fat along nerve and blood vessels from adjacent structures have been brought forward as possibilities of pathogenesis. Elkin and Hawthorn[19] have reviewed carefully the various theories of histogenesis and conclude that the question involved is whether the tumor is composed of true fat cells arising from a lipoblast or whether some other type of cell such as connective tissue cells has undergone fatty infiltration. They favor the lipoblastic origin of these tumors. Meyer and Sydel[20] believe they arise from displaced embryonic mesoderm. Starry[3] feels that they must represent either the type of connective tissue cells commonly found in the uterus or that they represent some specially differentiated type of lipogenic connective tissue cell. In reviewing these theories, it is noted that they form two groups, the question being whether lipomas of the uterus arise from a true fat cell, the lipoblast, or whether or not a metaplasia of a different type of cell occurs, it being infiltrated with fat globules and transformed into fat-bearing cells.

This instance of a fatty tumor of the uterus reveals a mass of fat-containing cells supported by connective tissue stroma and surrounded by a thin capsule of connective tissue and condensed uterine muscle. Nowhere in multiple sections of the primary tumor mass have there been discovered muscle, cartilage, or other tissue elements. All the cells are mature fat-containing units and nowhere can there be noted evidence of metaplasia or fatty degeneration. In direct contrast, the adjacent typical leiomyoma contains no fat-bearing cells or fatty change of any kind. The evidence presented is directed in favor of a true lipoma of the uterus.

REFERENCES

(1) *Petersen, A. J.:* J. Lab. & Clin. Med. **8:** 369, 1922. (2) *Preissecker, E.:* Wien. Klin. Wchnschr. **39:** 51, 1926. (3) *Starry, A. C.:* Surg. Gynec. Obst. **41:** 642, 1925. (4) *Dworzak, E. H.:* Ztschr. f. Path. **34:** 20, 1926. (5) *Bride, J. W.:* J. Obst. & Gynaec. Brit. Emp. **36:** 83, 1929. (6) *Engelhard:* Nederl. tijdschr. v. geneesk. **1:** 224, 1929. (7) *Lund, F. B.:* New England J. Med. **208:** 536, 1933. (8) *Muschik, A.:* Ztschr. f. Geburtsh. u. Gynäk. **105:** 444, 1933. (9) *Nordin, F.:* Hygiea (Festband) **100:** 384, 1938. (10) *Burger, P.:* Gynécologie **37:** 269, 1938. (11) *Glas, R.:* Zentralbl. f. Gynäk. **54:** 514, 1930. (12) *Hymphrey, A., and Mustard, R. L.:* Am. J. Obst. & Gynec. **36:** 159, 1938. (13) *Thaler, H.:* Arch. f. Gynäk. **134:** 350, 1928. (14) *Von Franque:* Verhandl. d. deutsch. gesellsch. f. Gynäk. **9:** 491, 1901. (15) *Merkel, H.:* Beitr. z. path. Anat. u. z. allg. Path. **29:** 274, 1903. (16) *Knox, J. H. M.:* Johns Hopkins Hosp. Bull. **12:** 318, 1901. (17) *Brunings:* Verhandl. deutsch. Gesellsch. f. Gynäk. **8:** 348, 1899. (18) *Lockyer:* Lewis, Practice of Surgery, Hagerstown, Md., W. F. Prior Co., Vol. XI. (19) *Elkin and Hawthorn:* Surg. Gynec. Obst. **25:** 72, 1917. (20) *Meyer, R., and Sydel, O.:* Ztschr. f. Geburtsh. u. Gynäk. **50:** 274, 1903.

VELAMENTOUS INSERTION OF THE UMBILICAL CORD

As a Cause of Fetal Death in a Twin Pregnancy

J. W. Records, M.D., Oklahoma City, Okla.

(From the Obstetrics Department of Wesley Hospital and the Department of Obstetrics of the University of Oklahoma School of Medicine)

THE term velamentous insertion of the umbilical cord refers to the condition existing when the vessels of the cord separate at varying distances from the placenta and reach their place of insertion in the placenta by running between the amnion and the chorion. The theory of causation of the anomaly most generally accepted is that advanced by Franque, namely, that in such cases in early pregnancy the most vascular part of the ovum may be in the decidua capsularis instead of in the decidua basalis, in which case the abdominal pedicle takes its origin from the former tissue. However, with the advance of pregnancy the decidua basalis becomes the most vascular area, the abdominal pedicle retains its original position, the vessels extending from its maternal end to the margin of the placenta.

The anomaly has been found to occur in from 0.4 to 1.25 per cent of placentas by various observers. It occurs more frequently in multiple than in single pregnancies.

CASE REPORT

A 26-year-old white housewife was first seen for prenatal care Sept. 18, 1939. Her last menstrual period began on July 2, 1939, and was normal. There were no previous pregnancies. The family history and the past history were irrelevant. The pregnancy was without serious complications. The blood, Kline and Wassermann tests as well as periodic urinalyses were negative.

At various intervals the systolic blood pressure varied from 90 to 122 and the diastolic from 50 to 68. The total weight increase was from 94 pounds to 118 pounds.

The diagnosis of twin pregnancy was made and confirmed by x-ray in the thirty-second week of pregnancy. On March 22, 1940 (thirty-fourth week), the membranes ruptured without previous labor pains and a considerable quantity of bright blood accompanied the escaping amniotic fluid. The duration of the bloody show was very short and on admission to the hospital one hour later there was only a small amount of blood-tinged discharge.

The blood pressure was 110/60, and she was beginning to have slight uterine contractions every five minutes. The head of the lower fetus was engaged, the position being right occiput anterior. The position of the upper fetus was transverse with the head in the left upper quadrant. Fetal heart tones were heard over most of the right side of the abdomen, both above and below the level of the umbilicus.

The labor proceeded normally for about seven hours when an umbilical cord was seen to be prolapsed from the vagina. The patient was put on the delivery table immediately and an attempt was made to replace the cord. The cord was pulseless, flaccid and green in color, giving the impression that it had been functionless for some time. Vaginal examination disclosed that the cervix was about four fingers dilated, and protruding from the external os was an intact bag of waters. This was ruptured and a large amount of meconium-stained amniotic fluid escaped. A firm fetal head immediately settled into the cervix.

Fetal heart tones were easily heard in the right lower quadrant and in no other locations. Attempts at complete reposition of the umbilical cord were unsuccessful, and when the cord was held up between the head and the cervix, releasing the pressure, no pulsation occurred. The patient continued in labor, the cervical os completing its dilatation rapidly, and about two hours after the prolapsed cord was first seen the head was visible for an extent of about 8 cm. in diameter. Delivery of a living male infant was then effected with low forceps after a small mediolateral episiotomy.

This infant's respiration was sluggish, and it required resuscitation with inhalations of oxygen and carbon dioxide mixture. Five minutes later a stillborn male infant was delivered spontaneously from right occiput anterior. This fetus obviously had been dead for several hours, its skin exhibiting a dark red discoloration and

several large areas of maceration. The fetal head was extremely soft. No other abnormalities were noted. Three minutes later the placenta was expelled without difficulty. There was no abnormal bleeding.

The infant delivered first weighed 1,518 Gm. (4 pounds 5 ounces). The stillborn infant weighed 1,320 Gm. (3 pounds 12 ounces). The placenta weighed one kilogram and was 20 cm. in diameter. The cord to the living baby was 48 cm. in length and was inserted eccentrically about 6 cm. from the edge of the placenta.

The cord to the stillborn fetus was 54 cm. in length, about one-half the diameter of the other one and was attached to the edge of the membranes; the umbilical vessels running between the two layers of the membranes for a distance of 8 cm. before entering the placenta. At a point near the entrance of the vessels into the substance of the placenta on the maternal side were seen two breaks in the vessel walls with hemorrhage between the membranes.

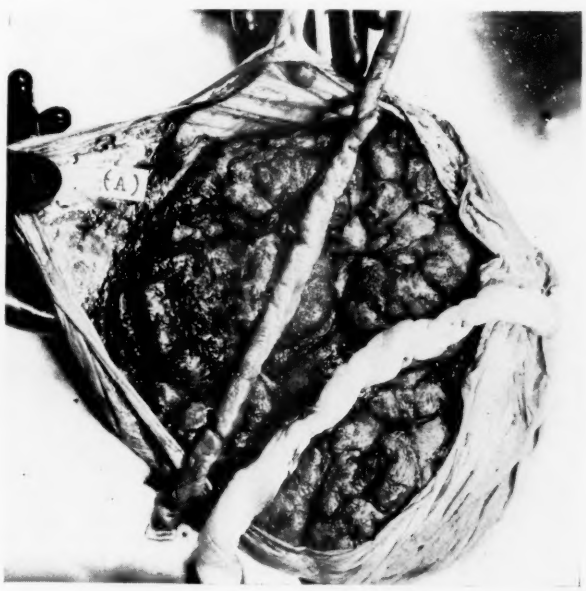


Fig. 1.—Maternal surface of placenta. Velamentous insertion of the cord (above) with point of rupture of umbilical vessels at *A*. Normal cord at right.

SUMMARY

A case is reported of velamentous insertion of the umbilical cord with rupture of the umbilical vessels, probably causing death of one fetus of twins in utero and onset of premature labor.

The possibility of fetal death resulting from rupture of the umbilical vessels in their course between the two layers of the membranes is illustrated by the case reported. The condition may be suspected when moderate bleeding and signs of fetal cardiac embarrassment or death appear at term with no evidence of placenta previa or premature separation of the normally implanted placenta.

REFERENCES

Kosmak, G. W.: Am. J. Obst. & Gynec. **16**: 438, 1928. *Boley, H. B.:* Ibid. **25**: 156, 1933. *Whitehouse, A. J.:* Ibid. **33**: 527, 1937. *Morehead, D. E., and De Carle, D. W.:* Proc. Staff Meet. Mayo Clin. **6**: 391, 1931. *Arey, L. B.:* Curtis' Obstetrics and Gynecology, Philadelphia, W. B. Saunders Company **1**: p. 472. *Schumann, E. A.:* Curtis' Obstetrics and Gynecology, Philadelphia, W. B. Saunders Company **1**: p. 506.

301 West 12th Street

PARALDEHYDE ANALGESIA AND PERINEAL ANESTHESIA IN OBSTETRICS*

C. K. Fraser, M.D., and J. W. Jones, M.D., Durham, N. C.

(From the Department of Obstetrics and Gynecology, George Washington University School of Medicine, Washington, D. C., and the Department of Obstetrics and Gynecology, Duke University Hospital, Durham, N. C.)

THE purpose of this paper is to present our clinical observations based on personal experiences in the use of paraldehyde analgesia with perineal anesthesia in terminating the second stage of labor.

We have also incorporated a series with complications of pregnancy and parturition in which other forms of analgesia were employed, but the delivery was accomplished with perineal anesthesia.

The incentive for our interest in this field was derived from two sources. W. Z. Bradford demonstrated the technique and the value of perineal anesthesia in obstetrics. H. F. Kane suggested the application of this obstetric refinement in terminating labors in which paraldehyde, as an amnesiac, has been employed.

The practice of blocking the pudic nerve was first used in Germany by Ilmer[1] in 1910. In 1913 it was introduced into this country by Gellhorn,[2] although he later gave it up for local infiltration. A relatively small number of papers have since appeared in the literature on this subject. King[3] in 1916 presented a very practical discussion on the anatomy of the female perineum and the technique of nerve block and infiltration. Torland,[4] Greenhill,[5] Bradford,[6] Ruth and Stiles,[7] Walker,[8] Ditter,[9] Urnes and Timerman,[10] have contributed papers which point to the advantages of perineal anesthesia in certain cases. All report good results whether nerve block, local infiltration or a combination of these methods was used.

METHOD

We have used a combination of nerve block and local infiltration. The patient is prepared and draped for delivery. The pubic arch and ischial tuberosities are palpated for orientation. A point on the skin midway between the rectum and ischial tuberosity is selected for the entrance of the needle. King[3] recommends spraying the site of puncture with ethyl chloride, others inject an intradermal wheal with a hypodermic needle. We have found their use unnecessary if the patient is under adequate analgesia.

If a perineotomy is to be done, the injection is made first on that side, for the action of the drug is more complete at the point of incision. A 22 gauge needle, 10 cm. in length, is inserted at the selected area and directed just medial to the ischial tuberosity.

With one finger in the vagina, the point of the needle is guided posterior to the ischial spine, care being taken not to pierce the vaginal wall. The needle is brought to rest proximally and posterior to the ischial spine. Traction is made on the plunger and if blood is not aspirated, 10 c.c. of a 1 per cent solution of procaine hydrochloride is injected. By withdrawing the needle 2 or 3 cm., some of the solution is deposited beneath Colles fascia where, as pointed out by King,[3] the anatomic arrangement of the fascia does not allow the solution to escape save anteriorly where it will bathe the terminal branches of the pudendal nerve anterior to the triangular ligament. The

*Read, by invitation, at a meeting of the Washington Gynecological Society, March 23, 1940, Washington, D. C.

needle is then withdrawn until the point is just beneath the skin. It is then inserted so as to infiltrate beneath the cutaneous and mucosal surfaces at the site of the perineotomy, and 10 c.c. of the solution is injected. The procedure is then repeated on the opposite side, omitting the local infiltration for incision.

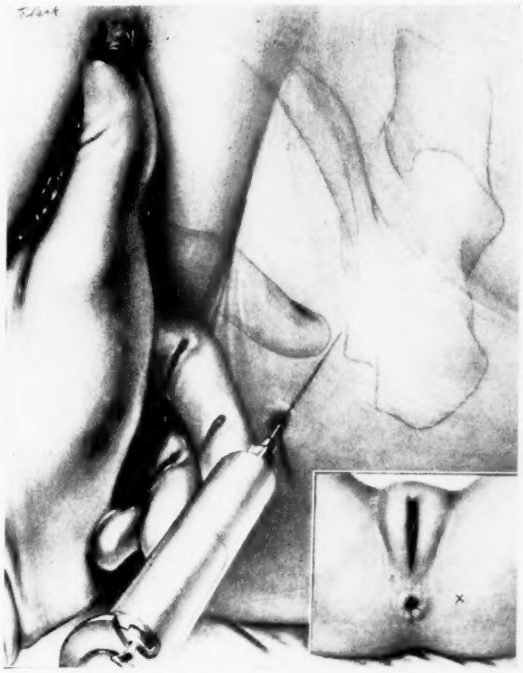


Fig. 1.—Point selected for insertion of needle. Needle brought to rest proximally and posterior to ischial spine.

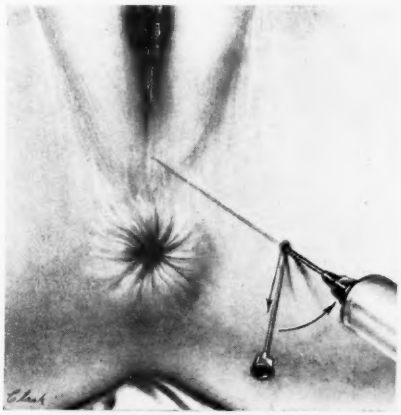


Fig. 2.—Infiltration at site of perineotomy.

By this method 50 to 60 c.c. of the anesthetic solution is adequate. As one becomes skilled in placing the solution, it will be found that smaller amounts are required. In a few cases, infiltration of the area selected for perineotomy was unnecessary, the bilateral nerve blocking giving complete anesthesia. However, we usually infiltrate this area and do not hesitate to use more of the solution if the anesthesia is not satis-

factory. In a few instances in which a deep perineotomy was utilized, there was some discomfort when the incision extended to the area supplied by the inferior hemorrhoidal and posterior cutaneous nerves of the thigh. In such cases the local infiltration may be augmented so as to include the posterior triangle as described by King.[3]

It will be noted that Table I includes uncomplicated cases, the majority of which are primiparas. All had paraldehyde analgesia. They were terminated with perineal anesthesia.

A series with complications of pregnancy and parturition is presented in Table II in which primiparas predominate. Other forms of analgesia were employed. All cases were terminated with combined nerve block and local infiltration.

TABLE I. PARALDEHYDE ANALGESIA

A. Parity:	
a. Primiparas	28 cases
b. Multiparas	3 cases
B. Position:	
a. Occipitoanterior	31 cases
C. Type of delivery:	
a. Perineal forceps and extraction	28 cases
b. Spontaneous parturition	3 cases
c. Perineotomy and repair	28 cases
d. Repair primary laceration	1 case

TABLE II. OTHER FORMS OF ANALGESIA

A. Parity:	
a. Primiparas	14 cases
b. Multiparas	6 cases
B. Position:	
a. Occipitoanterior	14 cases
b. Occipitotransverse	2 cases
c. Occipitoposterior	1 case
d. Right sacroanterior	3 cases
C. Complications of pregnancy and parturition:	
a. Eclampsia and active pulmonary tuberculosis	6 cases each
b. Arrested pulmonary tuberculosis, diabetes mellitus with acidosis and pre-eclamptic toxemia, lobar pneumonia, hypertension and cardiac failure, pre-eclamptic toxemia	1 case each
c. Frank breech	3 cases
D. Type of delivery:	
a. Perineal forceps and extraction	14 cases
b. Spontaneous parturition and breech extraction with Mauriceau-Smellie-Viet maneuver	3 cases each
c. Manual rotation O. T., to O. A.	2 cases
d. Perineotomy and repair	15 cases
e. Repair primary and second degree laceration	2 cases each
f. Repair sulcus laceration	1 case

SUMMARY

We feel that paraldehyde analgesia with perineal anesthesia has yielded satisfactory results in our hands.

It is our clinical observation that intra- and postpartum hemorrhage is decreased with this method. In one case a retroplacental hematoma necessitated administration of parenteral fluids. The uterus reacted well following completion of the third stage.

The immediate puerperium has been encouraging. As shown in Table I, no case required catheterization. There was no morbidity. All tolerated regular diets following parturition.

The relative cost of paraldehyde analgesia and perineal anesthesia in our hands is approximately 9 to 11 cents per delivery, a financial factor of some importance in many institutions.

We agree with Greenhill[5] that this method should not be used in the presence of local inflammation or in nervous, high-strung individuals.

The contraindications for general anesthesia in obstetrics are the indications for perineal anesthesia. This is well exemplified in our second table where forms of analgesia other than paraldehyde were used, but all cases were terminated with perineal anesthesia.

The authors wish to thank Drs. Bayard Carter, R. A. Ross, and H. F. Kane for permission to publish these cases.

REFERENCES

(1) *Ilmer, W.:* Zentralbl. f. Gynäk. **34:** 699, 1910. (2) *Gellhorn, G.:* J. A. M. A. **61:** 1354, 1913. (3) *King, R. W.:* Surg. Gynec. Obst. **23:** 615, 1916. (4) *Torland, T.:* Northwest Med. **29:** 312, 1930. (5) *Greenhill, J. P.:* South. M. J. **26:** 37, 1933. (6) *Bradford, W. Z.:* South. Med. & Surg. **98:** 19, 1936. (7) *Ruth, H. S., and Stiles, J. A.:* Am. J. Surg. New Series **32:** 217, 1936. (8) *Walker, A.:* Am. J. Obst. & Gynec. **32:** 60, 1936. (9) *Ditter, F. J. A.:* Northwest Med. **35:** 150, 1936. (10) *Urnes, M. P., and Timerman, H. J.:* J. A. M. A. **109:** 1616, 1937.

ACUTE INVERSION OF THE UTERUS POST PARTUM ASSOCIATED WITH PLACENTA ACCRETA

BÉLA HALPERT, M.D., AND PETER GRAFFAGNINO, M.D., NEW ORLEANS, LA.

(From the Departments of Pathology and Bacteriology and of Obstetrics and Gynecology of Charity Hospital of Louisiana at New Orleans and the Louisiana State University School of Medicine)

RECENT reports by Brett,[1] Peel,[2] Rucker,[3] Williamson,[4] Acosta-Sison and Mendiola,[5] Cosgrove,[6] Harer and Sharkey,[7] and Phaneuf[8] have discussed the principles involved in post-partum inversion of the uterus. Among the predisposing factors listed is placenta accreta, with or without manual separation.

In those tragic instances in which death occurs, permission for necropsy is not usually obtained and the anatomic cause of the inversion is therefore not ascertained. The case herein reported is the only instance in which such permission was obtained at the New Orleans Charity Hospital during the past twenty years. A reason for reporting this case lies in the fact that the chief cause, placenta accreta, is likewise unusual, and that fundal insertion of the placenta also played a part in the mechanism of inversion.

C. H., a 21-year-old, negro primipara, was first seen in the Outpatient Clinic of Charity Hospital of Louisiana at New Orleans Oct. 14, 1938. She was well developed, well proportioned, and well nourished. Delivery was expected in about two weeks. The patient complained of dyspnea on exertion, edema of the feet, and occasional nausea and vomiting. The blood pressure was 143/88. The fundus extended 29.5 cm. above the symphysis. Her pelvic measurements were within normal limits. The blood Wassermann reaction was negative.

The patient was admitted to the hospital Oct. 30, 1938. Labor began at 4 P.M. on the same day. The presentation was vertex. At 3:45 A.M. Oct. 31, 1938, a full-term child, weighing six pounds 15½ ounces, was delivered.

The placenta failed to separate and the patient began to bleed profusely from the uterus. An attempt was made to remove the placenta manually, but it seemed adherent to the superior and posterior lateral walls, and when it finally separated, inversion of the uterus followed, extending as far down as the introitus of the vagina. The uterus felt hard and contracted but was still bleeding. The vagina was packed, following which the patient's blood pressure dropped to 50/30 and her pulse rose to 140 per minute. Supportive treatment was of no avail and death occurred at 7:28 A.M. October 31, less than four hours after delivery.

At necropsy (A-38-1054) nothing unusual was noted about the head, neck, chest, and abdomen. The peritoneal surfaces were smooth and glistening, and there was no excess fluid. The uterus extended 7 cm. above the symphysis pubis. It was inverted and the fundus appeared sunken. The uterine ends of the Fallopian tubes and of the broad and round ligaments were drawn into the cavity formed by the inverted uterus.

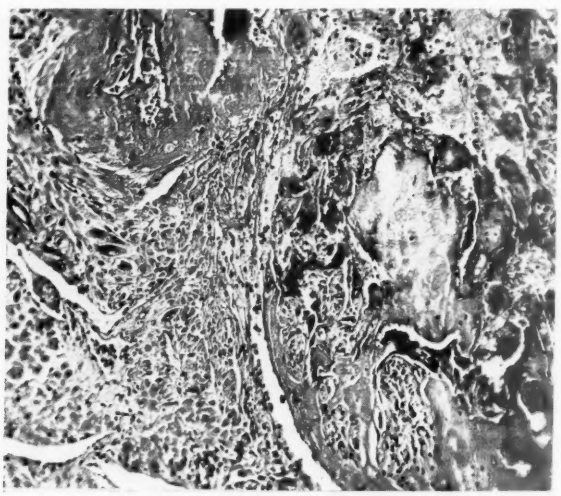


Fig. 1.—Preparation from the fundus of the inverted uterus showing remains of chorionic villi and the compact layer of the decidua with no spongy layer intervening between these structures and the myometrium.

The uterus measured 12 by 12 by 8 cm. The fundus was inverted and its raw inner surface protruded into the vagina. The broad ligaments and the Fallopian tubes were drawn in so that at the top the ampullary portions of the Fallopian tubes and the ovaries were near to one another. They were of usual size and appearance.

MICROSCOPIC EXAMINATION

Myocardium.—There was a slight variation in the size of the myocardial fibers; in places they appeared vacuolated and their striations were indistinct. Many of the nuclei stained deeply and an occasional one was bizarre in shape. The tissue elements appeared somewhat spread apart. No changes were noted about the blood vessels.

Lungs.—The lumina of some of the bronchioles contained pink-stained material with a number of polymorphonuclear leucocytes and large mononuclear cells. The mucosa appeared wrinkled. Some of the air spaces were collapsed and others wide open. The interalveolar septa were narrow in some places and fairly broad in others.

Examination of preparations of the spleen, liver, pancreas, suprarenal glands, kidneys, and mammary glands revealed no pertinent changes.

Uterus.—Preparations from the fundus of the inverted uterus disclosed remains of chorionic villi and the compact layer of the decidua with little or no spongy layer intervening between them and the myometrium (Fig. 1).

SUMMARY

A case is reported of acute post-partal inversion of the uterus in a 21-year-old negro primipara. The uterus was completely inverted and extended to the introitus, drawing in with the fundus the proximal ends of the Fallopian tubes, the mesosalpinx, and the broad and round ligaments. The attachment of the placenta was chiefly over the fundic portion, and microscopic examination disclosed placenta accreta, the placenta being adherent to the uterine wall, without an intervening spongy layer. The uterine inversion was thus caused by placenta accreta, the fundic attachment of the placenta, and perhaps the attempt at its manual separation.

REFERENCES

(1) *Brett, P. G.:* Med. J. Australia **1:** 254, 1938. (2) *Peel, J. H.:* J. Obst. & Gynaec. Brit. Emp. **45:** 821, 1938. (3) *Rucker, M. P.:* South. M. J. **32:** 197, 1939. (4) *Williamson, C. V.:* Bull. School Med. Univ. Maryland **24:** 32, 1939. (5) *Acosta-Sison, H., and Mendiola, N. D.:* J. Philippine Islands M. A. **19:** 395, 1939. (6) *Cosgrove, S. A.:* Am. J. Obst. & Gynec. **38:** 912, 1939. (7) *Harer, W. B., and Sharkey, J. A.:* J. A. M. A. **114:** 2289, 1940. (8) *Phaneuf, L. E.:* Surg. Gynec. Obst. **71:** 106, 1940.

SIMULTANEOUS OVARIAN AND INTRAUTERINE PREGNANCY

G. C. Milnor, M.D., F.A.C.S., and H. E. Bowles, M.D.,
Honolulu, T. H.

Pudney[1] has reported the simultaneous occurrence of a left ovarian pregnancy and a right tubal pregnancy, but a review of the literature available to us here fails to show any record of the coexistence of a primary ovarian pregnancy with a normal intrauterine gestation. We wish to offer the following case as one of this type. It fulfills Spiegelberg's criteria inasmuch as (1) the tube of the affected side was intact and had no organic connection with the gestation sac; (2) the fetal sac occupied the position of the right ovary; (3) the right ovary, containing the sac, was attached to the uterus by the ovarian ligament, and (4) definite ovarian tissue could be seen in the sac wall. Furthermore, the tube of the affected side showed no microscopic abnormality except for a slight edema.

Mrs. P., aged 28 years, was delivered of her fourth child on Jan. 19, 1939. All 4 pregnancies and deliveries were quite normal. Her past history was essentially negative except for a progressive otosclerosis as manifested by increasing deafness. Her menses began at thirteen and were normal every twenty-eight days except when she was pregnant. She had had no miscarriages.

On July 3, seven months after the birth of her last child, she was examined and found to be about two months' pregnant. Menstrual periods had begun two months after delivery. When seen, she had missed two periods and had the symptoms of pregnancy. She wanted an abortion, but this was refused and she was advised to have the child and be sterilized after the delivery. She was not seen again until August 23 at which time she gave the following history:

From July 3 until August 23 she felt quite well except for some nausea. At 1 A.M. on August 23 she was suddenly awakened with very severe abdominal pain. This grew worse and she fainted twice in an hour. She became pale and perspired profusely. There was also pain in her left shoulder, she vomited several times, and became dyspneic. When seen she was pale and in shock. The skin was cold and clammy, pulse 130, respiration 30, temperature 97° F., abdomen distended and very tender. A marked blueness was present around the umbilicus (Cullen's sign). Vaginally there

was great tenderness when the cervix was moved, and the cul-de-sac seemed to bulge. The uterus was enlarged and soft. Red blood count was 2,600,000, hemoglobin 67 per cent, white blood count 18,000, urine normal.

This appeared to be a typical picture of intra-abdominal hemorrhage caused most likely by a ruptured ectopic pregnancy. The uterus, however, was soft and larger than that usually found in simple ectopic pregnancies, and the diagnosis of intrauterine pregnancy on July 3 made the present diagnosis of ectopic gestation uncertain.

Under cyclopropane anesthesia an exploratory laparotomy was done. Five hundred cubic centimeters of citrated blood from her husband was given during the operation. More than two quarts of blood were present in the abdominal cavity. The right ovary was as large as a golf ball, black and distended at the upper pole. The tubes were grossly normal and the uterus was normally pregnant, from two and one-half to three months in size. The left ovary was normal. Six hundred cubic centimeters of blood was aspirated in citrate solution to be used for an additional transfusion if necessary. A rapid salpingo-oophorectomy was done, along with resection of part of the left tube for purposes of sterilization. As much as possible of the free blood and the large clots were removed before closing. The appendix was left alone.

Her condition immediately after the operation was better than at the start and in twenty-four hours she was in good condition. The intrauterine pregnancy was not disturbed, and she was delivered spontaneously of a normal, healthy, seven-pound seven-ounce, female infant after an easy labor on Feb. 29, 1940, six months after the operation for the ovarian pregnancy.

The pathologist's report on the removed ruptured ovarian pregnancy was as follows:

"*Gross.*—The specimen consists of an ovary which measures roughly 3 cm. in diameter. One-half of this is solid, and the other is cystic. The cyst is partly filled with blood clot and lined by a thin membrane which grossly resembles a gestation sac. In addition, a tube is present measuring 5 cm. in length and less than 1 cm. in diameter. Grossly it is approximately normal in appearance.

"*Microscopic.*—Sections taken through the ovary show a number of atypical, somewhat degenerated but unmistakable chorionic villi, most of them covered by two layers of cells. One or two small masses of decidual cells also appear. A section taken through the tube shows the mucosal folds normal in appearance and very little evidence of an active inflammatory process.

"*Diagnosis.*—Ovarian pregnancy."

SUMMARY

A case of ovarian pregnancy is herewith presented. It fulfills Spiegelberg's criteria and is of particular interest, because a coexisting intrauterine pregnancy was present. This latter went to term undisturbed. So far as we have been able to determine, there is no report of an identical case in the medical literature.

REFERENCE

(1) *Pudney, W. K.:* Am. J. Obst. & Gynec. 33: 161, 1937.

Vrba, K.: An Explanation for the Headaches Which Occur After Spinal Anesthesia, Monatschr. f. Geburtsh. u. Gynäk. 109: 285, 1939.

Headache follows spinal anesthesia in from 3.2 to 7.8 per cent of cases. They occur more often when operations are performed in the first half of the menstrual cycle, than in the second half or in the menopause. The author believes this is linked up with some action of the glands of internal secretion, especially of the hypophysis. The greater the concentration of pituitary hormone in the blood, the more frequent are the headaches. Likewise, headaches occurred more often during the spring and autumn, seasons in which there are pronounced atmospheric changes.

J. P. Greenhill.

TRAUMATIC HEMATOMA OF OMENTAL ADHESIONS SIMULATING PREMATURE SEPARATION OF PLACENTA

LOUIS J. ZUPP, M.D., AND VICTOR MAYER, M.D., WARREN, PA.
(From the Maternity Division, Warren General Hospital)

WE PRESENT a case which raised an interesting diagnostic problem. We realize the rarity of such a combination of factors but feel that there is likelihood of more frequent occurrence, in view of the increasing number of pregnant women coming to the delivery room with an abdominal scar as evidence of an earlier appendectomy or of pelvic surgery. The possible occurrence of hematoma of omental adhesions might well be considered in cases of trauma to the abdomen in late pregnancy where previous abdominal surgery has been done.

Mrs. J. B., aged 21 years, was brought to the Maternity Division of the Warren General Hospital on March 9, 1940, at 2:00 A.M., complaining of severe generalized abdominal pain. She had received no prenatal care during this, her second pregnancy. Her last mensis was dated vaguely during the middle of July, 1939, making this approximately her eighth month of pregnancy. Abdominal pain had begun about twelve hours prior to admission and was of increasing severity. There was nausea but no vomiting. (Several days later, the patient revealed that a short time prior to the onset of abdominal pain, she had become much alarmed when her baby developed convulsions, and she had rushed out into the open on an icy walk. She slipped and fell, striking her abdomen.)

Fifteen months prior to the present admission, the patient was admitted to the maternity division in labor with a full-term pregnancy. Examination at that time showed a generally contracted pelvis with direct evidence of cephalopelvic disproportion. Classical cesarean section was done and a live baby obtained. Convalescence followed a septic course with the patient developing a pyometra. Following a cautious dilatation of the cervix, with the institution of drainage, the patient recovered. She was discharged on the twenty-third hospital day in good condition.

Examination on admission disclosed a poorly developed and undernourished white female; heart and lungs normal; blood pressure 110/88. The size of the uterus was that of an eight months' pregnancy. The entire abdomen was exquisitely tender. The uterus felt very firm and as if persistently contracted. Fetal heart sounds were barely audible in the left lower quadrant. Fetal position was diagnosed as L.O.A. Pelvic measurements showed a generally contracted pelvis. Vaginal examination revealed a tender cervix with neither dilatation, effacement, nor bleeding. A diagnosis of premature separation of the placenta with concealed hemorrhage was made and immediate abdominal section planned.

A classical cesarean section was done. On opening the peritoneal cavity, the omentum was found adherent to the fundus and the anterior uterine wall. A large hematoma was present in the omentum overlying the uterus. No fresh bleeding points were evident. The omentum was separated from the uterus with ease. On opening the uterus, the cord presented and was not pulsating. The baby was delivered with some difficulty. No apparent abnormality was found in the placenta. The baby responded poorly to stimulation and died shortly afterward, although placed in a Drinker respirator.

The mother was returned to the ward in good condition. Her blood count at this time showed hemoglobin, 50 per cent; red blood count, 2,500,000; color index, 1; white blood count, 7,600; differential count: 86 per cent segmented polymorphonuclear leucocytes, 6 per cent nonsegmented polymorphonuclear leucocytes, and 8 per cent lymphocytes. She was given venoclyses of glucose in saline, and a transfusion of 600 c.c. of citrated blood. Convalescence was normal except for a transient

sapremia. The patient was discharged on the fourteenth postoperative day in good condition. The blood count at this time showed hemoglobin 78 per cent and red blood count 4,000,000.

We have presented a case of traumatic hematoma of omental adhesions in late pregnancy and wish to emphasize the ease in which this condition may resemble a premature separation of the placenta.

BILATERAL FIBROMA OF THE OVARIES COMBINED WITH A DEGENERATING ADENOMA OF THE RIGHT BREAST

EVA HAUMEDER, M.S., M.D., NEW HAMPTON, IOWA

(From the New Hampton Clinic)

FIBROMAS of the ovary, though not as uncommon as one might be led to believe by the scattered reports in the literature, are nevertheless an interesting finding, especially if the lesion is bilateral and combined with a degenerating cystadenoma of the breast.[1-5]

A white patient, 63 years of age, married, presented herself with complaints of pain and discomfort in the lower abdomen of about three to four weeks' duration.

Her menstrual history showed nothing unusual, having had her menarche at 13 years and menopause at the age of 50. She has three living children.

The physical examination revealed a well-nourished patient. The abdomen was enlarged, without rigidity or tenderness, by a movable, firm tumor in the lower quadrant, not connected with the uterus. There was no indication of the presence of ascites, no palpable glands, no edema. In the right breast a rather soft, nodular tumor, which was freely movable, could be palpated.

The patient was submitted to an exploratory operation at which time panhysterectomy was performed. The tumor in the right breast was removed at the same time. There was no fluid found anywhere in the body, neither abdominal nor pleural.

Pathologic Report.—The specimen consisted of uterus, both tubes and ovaries, also of the nodule from the right breast. The left ovary weighed 3,560 Gm. and measured 25 by 19 by 10.7 cm., and the right measured 10.5 by 8.4 by 6 cm. and weighed 1,520 Gm. The tumors were firm, showed a nodular surface, and were of grayish white color. On cut section the color was pearly white, glistening and of a coarse, fibrous, whirl-shaped structure. There were several yellowish areas of a softer consistency, as well as a cystic degeneration in the upper pole of the right ovary, measuring 5 by 4 by 3.9 cm. Signs of hemorrhage were also present. The left ovary was of the same structure and contained several much smaller cysts. The microscopic picture presented the usual structure of fibromas, interlacing bundles of fibrous tissue as well as a few muscle fibers. The large fibrous cells appeared mature with normal nuclei and comparatively small nucleoli and were arranged regularly. There were no mitotic figures seen. Some myxomatous and hyaline degeneration was present, as well as several areas of necrosis. The cysts showed a lining of a layer of flat epithelial cells.

The tumor of the right breast was a soft, hemorrhagic, nodular mass 4.5 by 3.5 by 3 cm. in size; on section it was cystic, reddish brown, gelatinous, and encapsulated. The microscopic pictures presented within a mucinous degenerated stroma a few glands, many dilated to cysts, the lining being a single layer of epithelial cells. There was marked round cell infiltration of the tissue as well as areas of hemorrhage.

The patient's recovery was uneventful, and after a period of five years, she is alive and well.

The tumor reported here did not cause any accumulation of fluid in the body, as is occasionally reported in the literature. It must have grown rather slowly because of the lack of symptoms and the patient's relative well-being. It would be interesting to speculate whether the tumor of the breast had any connection with the ovarian tumors, as ovarian tumors connected with changes in the mammary glands do occur.

REFERENCES

(1) *Clark, E. D., and Gabe, W. E.:* Am. J. Obst. & Gynec. **6**: 603, 1921. (2) *Fullerton, W. D.:* Surg. Gynec. Obst. **18**: 451, 1914. (3) *Hellman, A. M.:* Ibid. **20**: 692, 1915. (4) *Hoon, Merle R.:* Ibid. **36**: 247, 1923. (5) *Meigs, Joe Vincent, and Cass, John W.:* Am. J. Obst. & Gynec. **33**: 249, 1937.

VIABLE TRIPLETS DELIVERED BY CESAREAN SECTION

Linton Smith, M.D., and Don Cathcart, M.D., Atlanta, Ga.

(From the Crawford W. Long Memorial Hospital)

THE only report that we found in the literature of triplets being delivered by cesarean section with survival of all three babies, was by C. H. Roberts, in the *British Medical Journal*, July 2, 1927. We are, therefore, reporting our experience because of the rarity of such cases and, because of the uniqueness of identical boys with a triplet sister one month younger than they.

Case 91315.—The mother was a well-developed white woman, aged 29 years, who had been married eight years and had never been pregnant. Her health had been good except for infected tonsils for which a tonsillectomy had been done four years previously. She consulted one of us (L. S.) Feb. 10, 1939, after missing her second menstrual period, complaining of much nausea and vomiting. An examination showed her to be two months pregnant, which corresponded with her menstrual history. Her blood pressure was 119 systolic and 87 diastolic. Urinalysis was normal and Wassermann negative.

The nausea and vomiting persisted in spite of all treatment until the end of the seventh month which suggested an unusual degree of toxemia. At that time a careful examination showed a twin pregnancy with one fetus occupying a left occipitoanterior position, with the head rather low in the pelvis, and the other fetus in a breech presentation. An x-ray examination was not made for economic reasons and the presence of the third fetus was not recognized.

Dec. 6, 1938 being the first day of the last menstrual period, Sept. 12, 1939 was given as the expected date for delivery. The patient was seen weekly and her blood pressure and urinalysis at each examination revealed nothing abnormal, but on July 25 her blood pressure had increased from 119 to 140 systolic and 87 to 98 diastolic, and there was a small amount of albumin in her urine. She was placed on a milk diet and kept in bed. One week later her blood pressure had increased to 149 systolic and 104 diastolic, there was a large amount of albumin in her urine, and she was edematous. She was kept in bed, given a milk diet and saline purges, and an immediate termination of her pregnancy was suggested but declined.

On August 12 at 6 A.M. slight pains began, and she was taken to the hospital where she was given two ounces of castor oil and a hot enema followed by two minims of pituitrin subcutaneously every twenty minutes for four doses, but her pains continued irregular and weak. There was no dilatation of the cervix, and the lower uterine segment had not become obliterated. Her blood pressure was now 170 systolic and she was very edematous. No vaginal examination had been made, and a cesarean section was urged as she was considered definitely a preeclamptic. Two consultants agreed in the diagnosis and advised that an immediate operation be done. Both fetal heart sounds were of good quality, 150 and 156, respectively; the third fetal heart sound was not heard.

At 11 A.M. she was sent to the operating room and 150 mg. of novocaine were given intradurally, and immediate delivery by cesarean section was accomplished. On opening the uterus through a high left rectus incision, a male baby in the right occipitoanterior position was found and delivered; the other male baby which was in a breech position was then delivered. Both babies were in a common amniotic sac and their cords were attached to a common placenta. After

delivering the males, another fetus, a female, was discovered within a separate bag of water and with a separate placenta. The males weighed 4 pounds, 5 ounces, and 3 pounds, 10 ounces, and the female 3 pounds.

The males were apparently eight months' babies but the female, in addition to being much smaller, had the development of a seven months' fetus. The males breathed spontaneously. There was considerable difficulty in resuscitating the female, but after she began to breathe no further trouble was encountered. One of us (D. C.) assumed immediate charge of the triplets and at the end of six months they weighed 15 pounds, 8 ounces, 16 pounds, and 13 pounds, 6 ounces, respectively. They have never been ill since birth and are in excellent physical condition. On account of the economic condition of the family, the babies were kept in the hospital.

WEIGHTED ABDOMINAL RETRACTOR*

J. W. Visher, M.D., Evansville, Ind.

AN IMPORTANT problem in gynecologic surgery is retraction of the sigmoid and small intestines while operating upon the pelvic viscera. The Trendelenburg position is of considerable help, but in addition an abdominal roll of gauze is usually required to pack off the intestines. However, gauze is a foreign body which irritates the peritoneum and predisposes to postoperative abdominal distention and adhesions. Also, retraction is often inadequate as the intestines usually crowd down again into the operative field.

The retractor illustrated is the result of much study and experimentation. The curvature of the blade is similar to that of the female pelvis and fits into the cul-de-sac. The handle is forked, to prevent rotation, and the entire instrument is of sufficient weight (about three pounds) to hold back the intestine and leave an

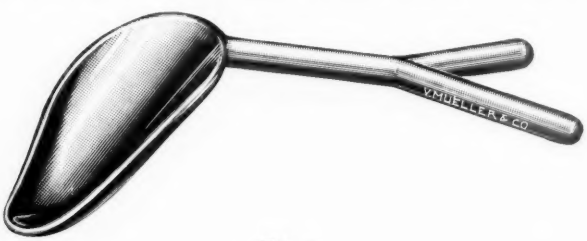


Fig. 1.

inch or more free working space between the uterus and the blade. The patient is placed in the Trendelenburg position, the abdomen is opened and a Balfour self-retaining retractor is inserted. The intestines are then pushed into the abdominal cavity, and the blade of the weighted abdominal retractor is placed in the cul-de-sac, while the handle rests upon the abdominal wall.

Its use facilitates all operations on the pelvic viscera, but it is especially valuable in hysterectomies. It can also be used in gall bladder operations. In addition to its value as a retractor, it has several other advantages. It protects the abdominal viscera from infection and collects the blood where it can be easily seen and removed. It decreases the manipulation of the intestines to a minimum, which materially decreases postoperative distention and adhesions.

---

*Manufactured by V. Mueller & Co., Chicago.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE TREATMENT OF PRE-ECLAMPSIA*

A RATIONALE FOR DIETARY REGULATION IN THE PRECLINICAL STAGE

GEORGE E. ANDERSON, M.D., F.A.C.P., BROOKLYN, N. Y.

MORE and more toxemia of pregnancy is becoming an "internist's disease," for its romantic ramifications into theoretical realms extend far beyond the scope of obstetrics and into the fields of metabolism, endocrinology, physiologic chemistry, and the pathologic physiology of such systems as the renal, the hepatic, and the vascular. No longer is the clinical work-up of any toxic gravida complete without a careful medical survey. It has been well said that toxemia of pregnancy is the "disease of theories," for its etiology and mechanism are still quite nebulous. It is likely that, in due time, it will be demonstrated that toxemia of pregnancy is a large group of diseases, with individual clinical pictures, each of which depends upon its respective percentage make-up of four main factors, the renal system, the endocrine system, the hepatic system, and the vascular system. One syndrome will be predominantly "liver," another vascular, another renal, another endocrine—but none in pure form.

The present consideration does not, except by way of differential diagnosis, include the chronic nephritides, states which are not toxemias of pregnancy at all since they antedated the gravid state and will continue to exist post partum—to be sure, with increased severity as a result of the unfortunate coincidence of pregnancy. There is little excuse in the carefully studied case for failure to recognize members of this nephritic group. The issue has unfortunately been beclouded by such an indefinable term as: "low-reserve kidney," which has often been used to cloak a bad differential diagnosis. The present consideration will touch on late pregnancy toxemia, the eclamptic group, or the toxemias of the last trimester of pregnancy. These are characterized: (1) by an inordinate gain of body weight throughout pregnancy—in the early months as latent water-retention, in the last trimester as frank edema; (2) by low or normal blood pressure in the early months followed by rather sudden climbing blood pressure in the last trimester; (3) by normal urinary findings in the early months, followed by frank albuminuria in the latter months of gestation. This group of signs may eventuate in anuria and convulsions at the time of reaching their peak, or they may, on the other hand, be sharply interrupted by a termination of the pregnancy, spontaneous or induced, whereupon there is characteristically a voluminous diuresis, gradual reduction in blood pressure, and a clearing of the albuminuria. This sharp diuresis

*Read, by invitation, at a meeting of the Brooklyn Gynecological Society, as part of a program on Maternal Mortality, May 3, 1940.

with rapid decline in albuminuria and blood pressure is, in a sense, a confirmation of the original diagnosis of the eclamptic type of toxemia, for the nephritides usually do not act in any such manner. When, on the contrary, after a typical episode of eclampsia or pre-eclampsia, there does not occur, following death of the fetus or termination of the pregnancy, a sharp diuresis, or when such signs as hypertension and albuminuria persist for six or more weeks post partum, one is usually dealing with a superimposed nephritis, or the condition has been a nephritis from the very beginning.

Progressive eye-ground and urinary findings should thereafter be watched for. Typically, the urine in the eclamptic group contains considerable albumin, mostly as serum-albumin, which usually boils solid just before the anuric stage is reached. There is in the pre-eclamptic patient usually a conspicuous absence of red blood cells in the urinary sediment, although hyalin and granular casts in showers are rather usual. The Addis urinary sediment count frequently presents a picture of nephrosis, namely, a marked increase in hyalin casts and albumin with a normal number of red blood cells. A 12-hour urinary red blood cell count above 500,000 suggests the presence of a concurrent hemorrhagic nephritis.

The blood chemistry in pre-eclampsia typically reveals a low nitrogen rest—a low or normal urea nitrogen, a high uric acid (often 5 mg. per cent or more), a tendency to low blood sugar, usually a high blood cholesterol until late in pregnancy,[1-5] when it may become low. Symptoms are sparse. They are, for the most part, dull headaches, spots before the eyes, and tightness of the rings on the fingers. The occurrence of marked headache and epigastric pain is often the herald of an approaching crisis. Young primiparas are most commonly afflicted, although older primiparas and, less often, multiparas suffer. The victims often show an endocrine anlage, such as hypothyroidism or that roundness of the hypopituitary individual.

Frequently, there is a history of previous food preference along the lines of carbohydrates rather than proteins,[6] such as meat, fish, eggs, and milk. The typical European breakfast of coffee and rolls and the "flapper" type of luncheon, soup, fruit salad, and tea, are found to be among the food habits of many of these patients. It may be of interest at this point to state that Ashe and Mosenthal[7] made a study, some time ago, of the average protein ingestion of nonpregnant adults in the New York area and, to their surprise, found that it was well below 50 Gm. daily, far below the accepted needs for the ordinary adult, not alone the gravid female who is building fetus and appendages and would obviously be obliged to tax her own body for the building stones.

Evidence is insufficient even to suggest that faulty diet is the cause of eclamptic toxemia; to date, there is no real evidence that the diet plays more than a contributory role. There can, however, be no doubt that a pregnant female, using a diet of 50 Gm. or less of protein, will be far more susceptible to water retention[6, 8-10] and edema than her more adequately nourished sister. One does not have to look to the pregnant state to establish this principle on a firm foundation; it is seen in cardiac patients with increased peripheral venous pressure. Even a slight diminution in the normal concentration of their plasma albumin or protein will, in the presence of a heightened venous pressure, swing these cardiac patients to the side of tissue edema. Certainly the pregnant woman, especially the primipara with firm rigid

abdominal wall, has the wherewithal for increased venous pressure. Add to this same rigid abdominal wall multiple gestation or hydramnios, complications long recognized as favoring eclamptic toxemia, and even the slightest discrepancy in plasma protein becomes greatly magnified in its significance in favoring tissue water retention. The careful and interesting work of Strauss,[6, 8] of Boston, has produced incontrovertible evidence of this.

While we do not know the cause of eclampsia, we are very cognizant of certain circumstantial disorders which accompany the syndrome, much as we are in the "set-up" of malignancy. We can, however, in eclampsia, employ far more rational therapy than in malignancy, and obviously we can more often steer a relatively safer course, despite our ignorance of etiology. Nebulous as may be our conception of its etiology, we should nevertheless employ *rational* therapy whenever possible, rather than empiric, unless it is found that the latter is definitely not harmful. Thus, the empiricism of colonic irrigation with bicarbonate of soda, of sweating the patient to make up for a supposedly deficient renal function, of imposing on her the burden of caloric or protein starvation, is of the past and is much in the same category as massaging an acutely inflamed appendix.

The toxic patient may *not*, in the light of even the meager knowledge available, be viewed as a *pure* nephritic problem or an endocrine or a metabolic problem, but must be viewed in a more collective sense.

The cause of water-logging in the eclamptic syndrome is not known; nevertheless, methods of treatment which encourage water retention should logically be avoided. First of all, sodium, whether this be in the form of sodium chloride, sodium bicarbonate, or sodium bromide, should be scrupulously reduced to a minimum, since its accumulation in the extracellular tissue spaces makes for water affinity. One occasionally sees patients placed on a salt-low diet of 2 to 3 Gm. daily and at the same time given sodium bromide by rectum at the rate of 4 to 6 Gm. a night for sedation. These same patients sometimes receive daily colonic irrigations of sodium bicarbonate in 5 per cent solution. Such divergent therapy could never pass any therapeutic rationalist. We used to fear the chloride ion and blame it for edema; now we commonly use chloride of ammonium and calcium chloride for their acidifying effects in order to produce diuresis and a mobilization of sodium from the tissue spaces.

The so-called "hydration method" of Newburgh,[11, 12] recently published by Alvarez, in which method unlimited amounts of water are given by mouth, is, in truth, a dehydration regime—since, under certain conditions, water is one of the best diuretics. The "hydration method" is effective in the pre-eclamptic patient *when ammonium chloride is concomitantly given*, for it mobilizes and washes out sodium in the presence of an acid diuresis. I can see no point, however, in insisting on a neutral ash diet and then thoroughly acidifying the individual with ammonium chloride. One can readily recognize the principle aimed at, namely, the avoidance of an alkaline ash diet which otherwise would favor water retention. The old vogue of alkalinizing the eclamptic patient by drug or diet is born of ignorance. Even the ketones occasionally found in the blood and urine of these patients late in their disease could be serving the purpose of dehydration rather constructively, if it were not for their known irritating effect on the renal tubules, thereby heightening any existing nephrosis. It goes

without saying that ketones, despite their dehydrating effect, should be destroyed in or removed from the body by adequate forced glucose utilization. Ordinarily, however, the careless unlimited administration of water is to be deprecated in the pre-eclamptic patient.

Among good empiric dietary measures employed in the past in pre-eclamptic toxemia is the copious use of milk. It may be stated without reservation that this has, inadvertently, saved many a life. Its high potassium and calcium content has favored diuresis. The protein content of one and one-half quarts of milk as usually prescribed approximates 50 Gm., making up, somewhat, for the protein starvation often otherwise purposely imposed by the medical attendant.

Just why should one's anxiety be so keen that the patient receive adequate protein in her diet? The old dictum that, since the patient is pouring out albumin in the urine, albumin-producing foods should be withheld, is as fallacious as was the principle of withholding sugar-producing foods from the diabetic patient because he is losing sugar in the urine. We now find that the diabetic individual does much better when he is receiving a liberal carbohydrate intake, whether or not he requires insulin. Several facts point to the extreme importance of making certain that the pre-eclamptic gravida is in nitrogenous equilibrium. First, she is building fetus, uterine muscle, and placental tissue; the building stones are better supplied than extracted from her own organism. Second, early in pregnancy the pre-eclamptic patient usually runs a low basal metabolic rate; protein, by its specific dynamic effect, tends to stimulate metabolism and thereby to burn off excesses of cholesterol. Late in pregnancy, these same patients frequently develop an accelerated metabolic rate far in excess of what would be represented by the additional gestational tissue; under such conditions of increased burning, there are greater protein demands on the maternal organism—they should certainly be supplied. Third, a progressive albuminuria is often found to cause some albumin depletion; it should be replenished to maintain within the vessels effective osmotic pressure and thereby forestall tissue edema.[6, 8] For these purposes animal proteins are far more efficient than vegetable proteins—at least 100 per cent more effective.

Let us next consider the case *against* protein feeding. That pathologic pictures identical with nephritis[13] have been produced in experimental animals by the feeding of animal protein cannot be denied. An excellent refutation to this argument, however, is the fact that white rats are herbivorous and certainly man does not fit into the same category. Besides, the amount of protein fed was enormous compared with man's intake. Today there is no worthwhile medical[14, 15] authority who denies his most severe nephritic patient at least a maintenance of animal protein. Whereas the nephritic patient on a protein-free diet formerly died prematurely by virtue of his physician's exacting diet prescription, today she lives just so long as her kidneys can carry on their function rather than so long as there still remain some of her own tissue proteins which she can use up in lieu of a deficient diet.

Let us feed our patient not an excess of protein but an amount adequate for her needs. Let us, however, also prevent unnecessary protein catabolism and breakdown by sparing the body proteins. One will thereby take the load from the renal excretory mechanism for urea excretion. This sparing can unquestionably be accomplished by supplying the patient with that great protein sparer, carbohydrate. The

normal human being will always, if it is available, metabolize carbohydrate in preference to, and more efficiently than, protein and fat. This truth is beautifully demonstrated in diabetic patients who will carry on and very successfully maintain body weight on several hundred calories less per day than ordinarily anticipated, provided most of the food ingested is in the form of carbohydrate.[16] On the other hand, if insufficient carbohydrate be given, the human being runs in negative nitrogenous balance since he is forced to break down his own tissue-protein as well as the ingested protein for energy purposes.

Whereas carbohydrate spares protein, this function is not the main advantage of a high carbohydrate intake for the pre-eclamptic or the eclamptic patient. The liver is generally regarded as at least one of the "shock tissues" in eclampsia. It bears the brunt of wear and tear even through normal pregnancy as is evidenced by the fact that practically every liver in pregnancy is a fatty liver, much as is the liver in animals receiving large injections of "pituitrin."[17] Whenever fat fills the liver, the ability of that organ to store glycogen is usually greatly impaired. The early hypercholesteremia of those patients who are destined to suffer from pre-eclampsia predisposes to fat deposits in the liver, much as it does in diabetic patients, who, incidentally, are also very prone to develop the eclamptic syndrome. There is good evidence that one can,[18, 19] to a certain degree, delay or even prevent this lipoid accumulation in the liver by forced carbohydrate feeding and utilization (which really means forced glycogen storage in the liver). Hypercholesteremia does play a role in toxemia of pregnancy, possibly, as Colvin and Bartholomew[1-3] have suggested, by way of predisposing the patient to placental infarcts. Much has lately been written about these infarcts[20] and the roles of argenine and guanidine, arising therefrom, in producing the smooth-muscle phenomena of pre-eclampsia and the convulsive state. The theory is very interesting, but why do not otherwise normal pregnant women who not infrequently develop[21] placental infarcts go into eclampsia? The answer does not seem to be too difficult—it is probably because normal pregnant women still have livers which can deaminize and destroy these toxic amines more efficiently than can the damaged liver of the pre-eclamptic patient. There are good reasons for incriminating the liver in the eclamptic syndrome: (1) blood uric acid is high in these patients at a time when there is no inability of the kidneys to excrete this substance; (2) blood urea is characteristically low (the liver is the only organ in the body which can elaborate urea, and presumably in the eclamptic patient it is not succeeding well in doing so)—some of the lowest ureas on record are met in fatal cases[22] of eclampsia; (3) true eclampsia is far too frequently associated with the post-mortem findings of liver damage for such pathology to be mere coincidence.

Apart from pregnancy, it has been taught that carbohydrate[18, 19] is one effective agent available to protect the liver; when glycogen is heavily stored therein, this organ becomes less vulnerable. Witness the development of liver cirrhosis in long-standing, uncontrolled hyperthyroids[23] and other states in which an abundance of suprarenalin constantly makes the liver drop out into the blood stream, as glucose, its stores of glycogen. While glycogen can coexist in the liver with fat, it is most usual to find one present at the expense of the other. One of the few means we have at our disposal for safeguarding the liver is adequate carbohydrate ingestion (or parenteral glucose).

Bartholomew[1] has suggested burning-off the excess of cholesterol in the blood by thyroid feeding *early* in pregnancy, since there is usually at this time a low basal metabolism. It is doubtful whether thyroid in these patients would have any more effect than it does in typical lipoid nephrotics, patients who are notoriously resistant to this hormone. Moreover, thyroid feeding in pre-eclamptic females is not a new concept by any means, nor has it in the past been too successful in improving the clinical picture of the toxic patient. The thyroid discrepancy is not necessarily intrinsic in the thyroid gland; one must bear in mind that the very lowest[24] metabolic rates known to science come in association with destructive diseases of the anterior lobe of the pituitary gland. Unfortunately, the scope of this paper will not permit a consideration of the endocrine implications of the subject. I cannot, however, leave the endocrine field without stressing at least one practical point learned by sad experience—that there *may* be something in the original work of Hofbauer[25-29] in 1918 in respect to the posterior pituitary as being an etiologic factor in eclampsia. "Pituitrin" is so definitely antidiuretic that it is without doubt the most effective agent available for therapy of the polyuria occurring in diabetes insipidus. Dieckman, Michel,[30] and others have shown that patients suffering from the toxemias of pregnancy are extremely sensitive to the vascular-constricting and antidiuretic effects of "pituitrin." Best,[31] of insulin fame, has pointed out that the same type of fatty liver which occurs in pregnancy can be artificially produced in animals by repeated injection of "pituitrin." One should derive a certain moral, even without further evidence, that "pituitrin" or its analogues should never be used in any toxic female or in anyone who in previous pregnancy had pre-eclampsia or eclampsia. I am thoroughly convinced that I have seen deaths occur in pre-eclampsia as a result of acute renal shutdown incidental to even a single dose of "pituitrin" in a highly sensitive individual.

The importance of the endocrine system, the pituitary, the estrogen group,[32] estriol, etc., may ultimately furnish the solution of the problem of etiology in eclampsia. Certainly, it cannot be discarded as being an unrelated factor any more than can the liver.

What is the status of the vascular and renal systems in this disease? It has been suggested that they suffer *from*[34] the disease, rather than that they *cause* the disease. It is likely that the effect of the toxemia on these tissues actually determines whether the victim goes into convulsions or "rides out the storm" for the time being. Vascular spasm is the *effect*, not the cause. To be sure, if the spasm lasts long enough, it will be translated into permanent vascular damage and gross pathology. Intracranially this spasm seems in some way to be linked up with edema in producing the convulsive state of eclampsia.

Herrick and Tillman[33] feel that renal disease is the *result* rather than the *cause* of the eclamptic syndrome, that the differentiation between mild nonnephritic and severe nonnephritic toxemia is merely a matter of degree rather than kind. From their statistics, one may anticipate that more than half of those who suffered from eclampsia and are still alive three years after their toxic episodes will show evidence of permanent hypertensive vascular disease. It is the *ultimate* renal and vascular damage that one should consider in evaluating the status of the toxic female—what will she show or where will she be

in five or ten years hence, if one "pig-headedly" insists on her carrying to certain viability? What price a viable baby?

On the basis of these concepts, how can one rationally treat the pre-eclamptic female? The first step in treatment is of course a correct diagnosis. If, early in pregnancy, there is a hypertension with cardiac hypertrophy, the patient is obviously not suffering from pre-eclampsia, but in all probability from a so-called essential hypertension or a chronic nephritis. Continuation of the pregnancy, should, in the best interests of the patient, be discouraged. She is not entitled to even a trial of pregnancy if her future is to be considered unless with a full knowledge of the possibilities she would desire to gamble. Especially is the continuance of pregnancy to be deprecated if the patient shows an abnormal Addis count, or a faulty urea clearance, or a pyelitis, or a pyelonephritis (Zimmermann and Peters[34]). If one would put credence in Goldblatt's[35] theory of renal ischemia as producing essential hypertension, then by virtue of the possibility of pressure phenomena incidental to pregnancy one should recommend interruption in all cases of early hypertension whether or not there be concomitant renal findings.

The pre-eclamptic patient presents a far different picture. There is more of a range of safety in her case, although one must accept the fact that even she stands a "fifty-fifty" chance of premature vascular disease or early demise from a hypertensive vascular disease within a few years after her toxic episode.

The treatment of pre-eclampsia should really be started *before* the disease actually has developed in the individual. One should watch for and scrutinize the vagotonic type of patient with low blood pressure with vasospastic cold extremities, with spastic retinal vessels,[1] with slow or irritable pulse, and a history of bowel crises, especially if that patient is of the round hypopituitary or of the hypothyroid type. If she, in addition, carries a high cholesterol, a low or low-normal basal metabolism, a low blood sugar, and with the onset of pregnancy if she shows a rapid gain in body weight, she should be considered a very likely candidate for pre-eclampsia. Dietary treatment should *immediately* be instituted rather than waiting for the development of hypertension, albuminuria, or frank edema. She should receive at least the protein intake as recommended by The Technical Commission of The Health Committee on Nutrition for the League of Nations, 1.5 to 2.0 Gm. of protein per kilo, or for the 132-pound female, 90 to 120 Gm. Since much of the protein in the average diet is plant-borne, and therefore certainly less efficient, it is probable that an arbitrary figure of 150 Gm. of protein is more satisfactory, of which 110 Gm. should be as animal protein. The carbohydrate of the diet should be close to normal, namely, 300 to 350 Gm. Fat should be low, from 55 to 60 Gm. The diet should be low in sodium chloride (2 Gm. daily or less), high in calcium and potassium by virtue of a liberal milk allowance, and should meet Sherman's optima for vitamins. Vitamin D and the vitamin B complex will to advantage be added. Such a diet will range between 2,295 and 2,540 calories (Table I).

A diet of this sort will not favor water retention, will adequately glycogenize the liver, will tend to prevent hypercholesteremia, will supply unsaturated fatty acids so essential to the economy of all human beings, will furnish adequate protein for building the tissues of gestation, or for stimulating a sluggish metabolism through its specific

TABLE I. COMPARISON BETWEEN THE VALUES OF THE AVERAGE NORMAL DIET AND THE DIET RECOMMENDED IN PRE-ECLAMPSIA*

CARBOHYDRATES	PROTEINS	FAT	CALORIES
	Average Normal Diet		
350	70-100	90-100	2,500 to 2,700
	Diet in Pre-eclampsia		
300-350	150	55-60	2,295 to 2,540

Animal Protein About 110 Gm. Daily—Represented by

		PROTEIN VALUE	
Whole milk	1 pint	15.8	112 Gm. (animal)
Skim or buttermilk	1 pint	16.3	
Egg	One	5.9	
Meat (very lean) or Fish	½ lb.	74.4	
Vegetable protein		38.0	
	Total	150 Gm.	

In order that fat and cholesterol may be kept at low levels, avoid more than 1 egg daily, or more than 3 teaspoonfuls of butter, or 3 tablespoons of heavy cream, or the following high cholesterol-containing meats:

Pork, duck, goose, brains, sweetbreads, corned beef, canned tongue, butterfish, halibut, tuna, mackerel, smoked halibut, smoked herring, canned sardines, salmon, roe.

*In The Brooklyn Hospital, "Diet Control" by Anderson and Eschweiler is used to establish these values in menu form.

dynamic heat effect, and also for maintaining a normal level of blood plasma protein. Weight gain will usually remain normal on this diet.

On such a regimen many a predisposed individual will evade pre-eclampsia, which should if possible be treated long *before* it becomes clinically evident. By the same token, it is likely that after the development of albuminuria, hypertension, and gross edema, diet will accomplish very little from a corrective standpoint, since the necessary time factor for correction is too short. On the development of gross signs of pre-eclampsia, the patient should, of course, be hospitalized. The diet should be continued, with proportionately *more* milk than meat in order to favor diuresis and to replenish (if depleted) blood cholesterol, provided, of course, an increased metabolic rate, as is usual at this time, has supervened. If anemia is present, blood transfusion is in order. If plasma proteins are found to be even slightly reduced in amount, they should be replenished by serum or blood transfusion.

If after a two- or three-week period of diet, bed rest, and intelligent expectancy, there is not marked amelioration of all signs, or if there is a progression in *any* of the signs, induction of labor should be advised in the interest of the mother and her future life-expectancy. Procrastination beyond a three-week period is hazardous and may result in irreversible, irreparable renal or vascular damage.

It has been stated, as applied to uterine hemorrhage: "The only safe uterus is an empty uterus." When the toxic gravida does not rapidly respond to rational therapy, it would seem that the *same* principle should certainly be invoked.

REFERENCES

(1) *Colvin, E. D., and Bartholomew, R. A.:* AM. J. OBST. & GYNEC. **37**: 584, 1939. (2) *Bartholomew, R. A.:* J. A. M. A. **111**: 2276, 1938. (3) *Bartholomew, R. A., and Colvin, E. D.:* AM. J. OBST. & GYNEC. **36**: 909, 1938. (4) *Dieckmann, W. J.:* Arch. Int. Med. **53**: 71, 188, 540, 1934. (5) *Idem:* AM. J. OBST. & GYNEC. **26**:

543, 1933. (6) *Strauss, M. B.* (Boston): Am. J. M. Sc. **190:** 811, 1935. (7) *Ashe, B. I., and Mosenthal, H. O.:* J. A. M. A. **108:** 1160, 1937. (8) *Strauss, M. B.:* Am. J. M. Sc. **194:** 772, 1937; **195:** 516 and 723, 1938; **196:** 188, 1938. (9) *Dodge, E. F., and Frost, T. T.:* J. A. M. A. **111:** 1898, 1938. (See discussion by Addis, T.) (10) *Harden, Boyd:* A Study in Pre-Eclampsia and Eclampsia, 1936, University of Pittsburgh. (11) *Alvarez, R. R. D.:* Am. J. Obst. & Gynec. **39:** 476, 1940; *Newburgh, L. H., and MacKinnon, F.:* Practice of Dietetics, New York, 1934, The Macmillan Co., Chap. XII. (12) *McPhail, F. L.:* J. A. M. A. **111:** 1894, 1938. (13) *Farr, Smadel:* Proc. Soc. Exper. Biol. & Med. **36:** 472, 1937; *Howard:* J. A. M. A. **109:** 1654, 1937. (14) *Cameron, J. D. S.:* Ibid. **113:** 520, 1939. (15) *Reutmann, McCann:* J. Clin. Investigation **11:** 973, 1932. (16) *Rabinowitch, I.:* J. Nutrit. **16:** 549, 1938. (17) *Best, C. H., and Campbell, J.:* J. Physiol. **92:** 91, 1938; **94:** 47, 1938. (18) *Best, C. H.:* Lancet **1:** 1155, 1934. (19) *Althusen:* J. A. M. A. **100:** 1163, 1933. (20) *Young:* J. Obst. Brit. Emp. **26:** 1, 1914. (21) *Hartman, F. W.:* J. Obst. Brit. Emp. **34:** 279, 1927 (Discussion of Paper 2). (22) Personal experience of writer—a case in which blood urea before death reached 7 mg. per cent. (23) *Beaver, D. C., and Pemberton, J. deJ.:* Ann. Int. Med. **7:** 687, 1933. (24) *Silver, S.:* (Review of Simmonds' Disease) Arch. Int. Med. **51:** 175, 1933. (25) *Goodall, J. R.:* Am. J. Obst. & Gynec. **26:** 560, 1933. (26) *Hofbauer:* Abst. Am. J. Obst. & Gynec. **37:** 903, 1939. (27) *Teel, H. M., and Reid, D. E.:* Endocrinology **24:** 297, 1939. (28) *Gilman, A., and Goodman, L.:* J. A. M. A. **109:** 1545, 1937; J. Physiol. **90:** 113, 1937. (29) *Anselmino, K. J., and Hoffmann, F.:* Klin. Wchnschr. **10:** 1438, 1931. (30) *Dieckmann, W. J., Michel, and Woodruff:* Am. J. Obst. & Gynec. **36:** 408, 1938. (31) *Best, C. H., and Rideout, J. H.:* Am. J. Physiol. **122:** 67, 1938; Ann. Rev. Biochem. **8:** 349, 1939. (32) *Taylor, H. C., and Scadron, E. N.:* Am. J. Obst. & Gynec. **37:** 963, 1939. (33) *Herrick, W. N., and Tillman, A. J. B.:* Ibid. **31:** 822, 1936; Arch. Int. Med **55:** 643, 1935. (34) *Zimmermann, H. M., and Peters, J. P.:* J. Clin. Investigation **16:** 397, 1937. (35) *Goldblatt, H.:* Bull. New York Acad. Med. **14:** 523, 1938; Ann. Int. Med. **11:** 69, 1937. (36) *Wood, J. E., Jr., and Nix, H.:* J. A. M. A. **110:** 332, 1938. (37) *Peters, J. P.:* Ibid. **110:** 329, 1938.

451 Clinton Avenue

Books Received

COMPLETE GUIDE FOR THE DEAFENED. By A. F. Niemoeller. 256 pages. Harvest House, New York, 1940.

HANDBOOK OF HEARING AIDS. By A. F. Niemoeller. 156 pages. Harvest House, New York, 1940.

IMMUNE BLOOD THERAPY OF TUBERCULOSIS. By Joseph Hollos, M.D. 195 pages. Bruce Humphries, Inc., Winchester Street, Boston, Mass.

BIOCHEMISTRY OF DISEASE. By Meyer Bodansky, M.D., and Oscar Bodansky, M.D. 684 pages. The MacMillan Company, New York, 1940.

DIE GEBURTSHILFLICHEN OPERATIONEN. Ihre Ausfuehrung und Anwendung. Von Professor Dr. med. Heinrich Martius, Direktor der Universitaets-Frauenklinik Goettingen. Second revised edition, with 281 illustrations, part in color. 286 pages. Verlag von Georg Thieme, Leipzig, 1940.

SEX IN MARRIAGE. By Ernest R. Groves and Gladys Hoagland Groves. New revised edition. 250 pages. Emerson Books, Inc., New York, 1940.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

STILLBIRTHS AND NEONATAL DEATHS*

SCOTT C. RUNNELS, M.D., AND BURDETT WYLIE, M.D., CLEVELAND, OHIO

INTEREST has been centered on the problem of maternal mortality and the conservation of the older child to such an extent that the losses of babies at and shortly after birth have been largely neglected. The sources for this study are the various reports of the Bureau of the Census and monthly reports sent by a group of 46 hospitals to the Hospital Obstetric Society of Ohio.

The first problem is one of definition, as the terms stillbirth and neonatal death are indefinite and have different interpretations. The Census Bureau points out that the meaning of stillbirth is fixed by law in 25 states, by ruling of the State Board of Health in 22, by the local registrars in Pennsylvania, and by a letter defining the term to the doctors in Maryland. In the 25 states in which the definition is fixed by law, the term "advanced to the fifth month" is used in 21, with the exception that in the City of New York any product of conception is required to be registered, although the state legally defines the term as "advanced to the fifth month." The four states that are out of line are Connecticut which defines a stillbirth as a conception of "not less than twenty-eight weeks," in the District of Columbia the law is "passed the fifth month," in Indiana "seven months and over" and in the State of Washington "beyond the seventh month."

It would simplify the matter if the four states whose laws are not in accord with those of the 21 would amend their statutes. The situation is much simpler in the other 24 states. Here, merely an alteration in the ruling of the Board of Health would suffice. Delaware and New Hampshire have no definite ruling, Maryland and Missouri consider any dead product of conception a stillbirth, Idaho reports at four months, Kentucky, Ohio, and Massachusetts at four and one-half months, Montana and Pennsylvania after the fourth month, Maine, New Jersey, South Carolina, Vermont, Virginia, Wyoming at five months, Wisconsin after the fifth month, Nevada and Utah six months, Rhode Island after the sixth month, Kansas past the twenty-eighth week, and North Dakota does not report stillbirths until the seventh month. Any interpretation of stillbirth statistics must bear in mind the source of the material before evaluation.

The term neonatal deaths is also indefinite, being defined as "death in the newborn." As commonly used it means the death of the baby before the mother has left the hospital. In the reports from Ohio hospitals, given later in this paper, it is used in this sense. This is the most likely time of death, and while the time of hospital stay is indefinite, it would probably be prolonged if the child showed any reason for anxiety. However, that definition will not be practical in studying cases taken from statistical tables, so for the cases analyzed from the Census Bureau reports we have considered deaths in the first month as neonatal. Infant mortality includes all deaths within the first year. The purpose of this study is to bring into clearer definition the essential differences between deaths occurring shortly after birth and those occurring later.

Turning now to the number of stillbirths and neonatal deaths occurring in the United States, we find that in 1937 for every 1,000 live births there were 33.4 stillbirths and 33.3 deaths within the first month. Or stated another way, out

*Read at the Annual Meeting of the Hospital Obstetric Society of Ohio, Columbus, Ohio, April 3, 1940.

of every 100 pregnancies that approach term, there is a loss of 6.45 per cent of the babies before the end of the first month. The distribution of these losses by states is pictured in Charts 1 and 2. Stillbirths have decreased from 86,466 in 1930 with a rate of 39.0 per 1,000 live births, to 73,467 in 1938 with a rate of 32.0. Neonatal deaths have fallen in number from 78,182 in 1930 with a rate of 35.7 per 1,000 live births to 73,311 in 1937 with a rate of 33.3. The distribution of these improvements by states is shown in Charts 3 and 4. The general improvement in infant mortality has been shown by the Children's Bureau in their publications. This demonstrates that there has been greater improvement in child care in the cities than in the rural districts.

Segregating the infant deaths occurring in the first month of life we find that the improvement in infant mortality in the later months has been greater than that in the first month.

Distributing infant deaths according to the time following birth at which they occur it becomes apparent that the longer the child lives the more chance it has of continuing to live. There are more deaths in the first day following birth than there are in the rest of the first week and more deaths in the first week than there are in the last eleven months of the first year.

The distribution of stillbirths according to the month of gestation cannot be done so satisfactorily from a statistical point of view because of the irregularity of reporting stillbirths. However, the data in Table I were taken from figures reported by the Census Bureau from 7 states and 2 cities for the years 1935 and 1936. Of the states Connecticut and Washington report stillbirths only after

TABLE I. STILLBIRTHS BY MONTH OF GESTATION IN SEVEN STATES AND TWO CITIES

Connecticut, Illinois, New Jersey, New York, Oregon, Washington, Baltimore, and District of Columbia
1935-1936

Under 4 months	737	2.4%	
4 Months	1,381	4.5%	
5 Months	2,526	8.2%	
6 Months	3,397	11.0%	
7 Months	4,335	14.0%	40.1%
8 Months	7,031	22.8%	
9 Months	9,237	29.8%	52.6%
10 Months and over	247	0.8%	
Unknown	2,007	6.5%	
	30,898		

seven months; the rest fall in the group reporting in the fifth month. Reclassifying the same cases on the basis of reasons for death, we will take the longer list given by the Census Bureau of the cause for these stillbirth deaths and regroup them on an etiologic basis. For comparison we also list the fewer stillbirths derived from the reports of the Ohio hospitals for the year 1938.

With a few exceptions there is a fairly close analogy between the figures presented by the Ohio Hospitals and those of the Census Bureau. The two notable exceptions are the headings "death in utero" and the indefinite group in both of which the matter of classification could well have bearing. It is not to be expected that any really definitive classification can be arrived at until a fairly large number of cases in which autopsies have been done are accumulated. It has been the experience of the authors that several inexplicable intrauterine deaths have been found to be due to such causes as antepartum fetal pneumonia, and asphyxia has been found to be a congenital absence of the trachea. The Census reports can be no more accurate than are the death returns filed by the attending physicians. However, from year to year the accuracy of the returns is improving and the analogy between the more definite causes in the two lists published is close enough so that they are mutually confirmatory.

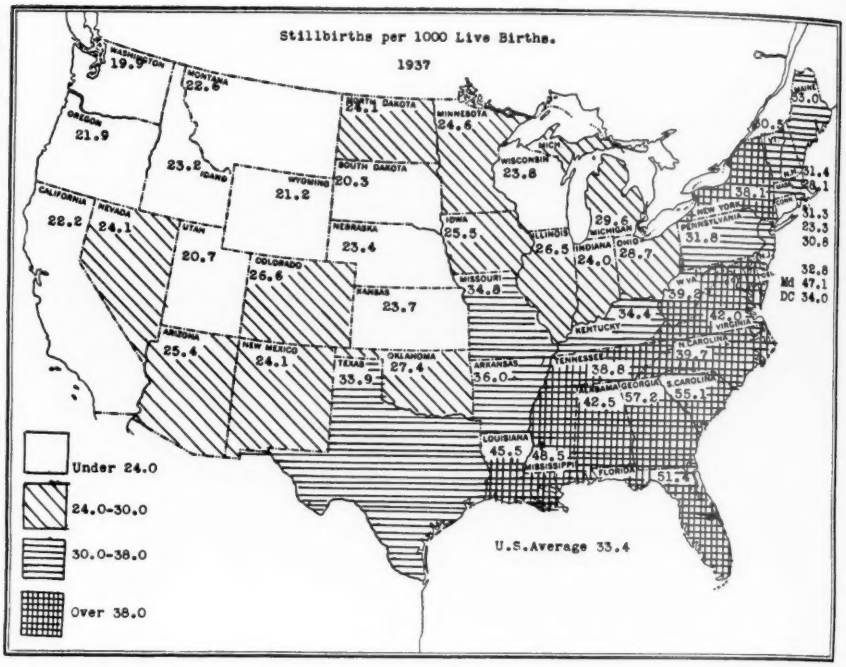


Chart 1.

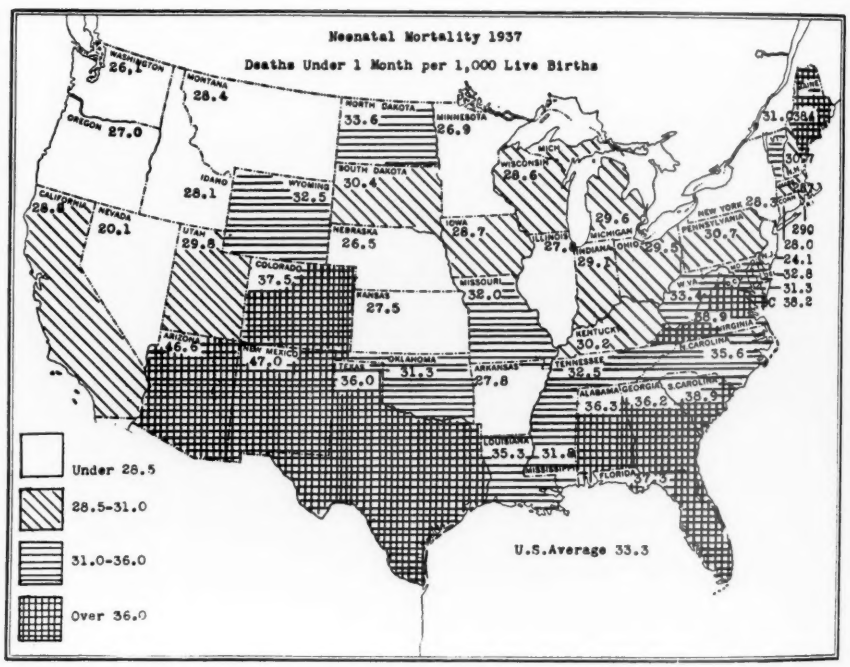


Chart 2.

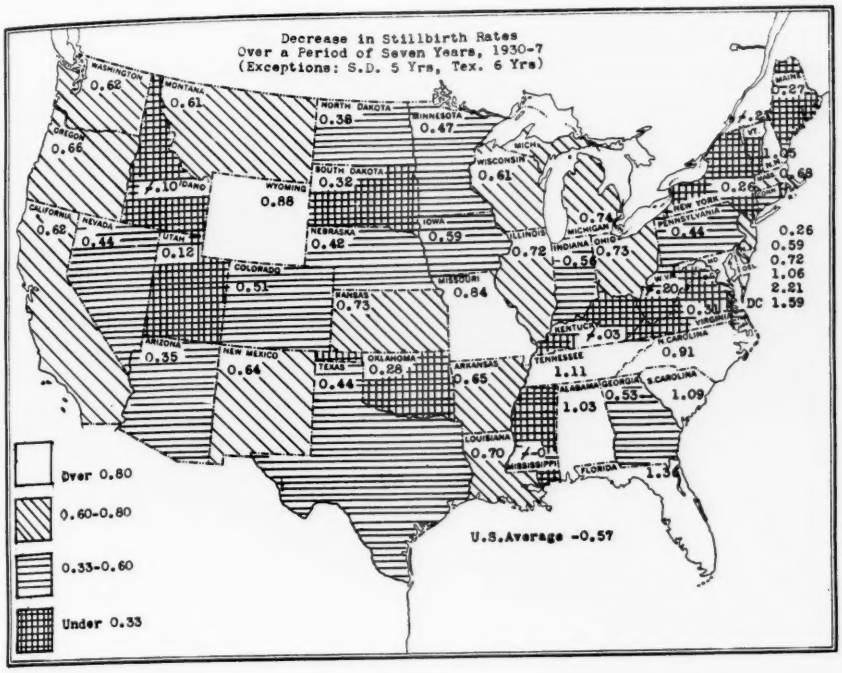


Chart 3.

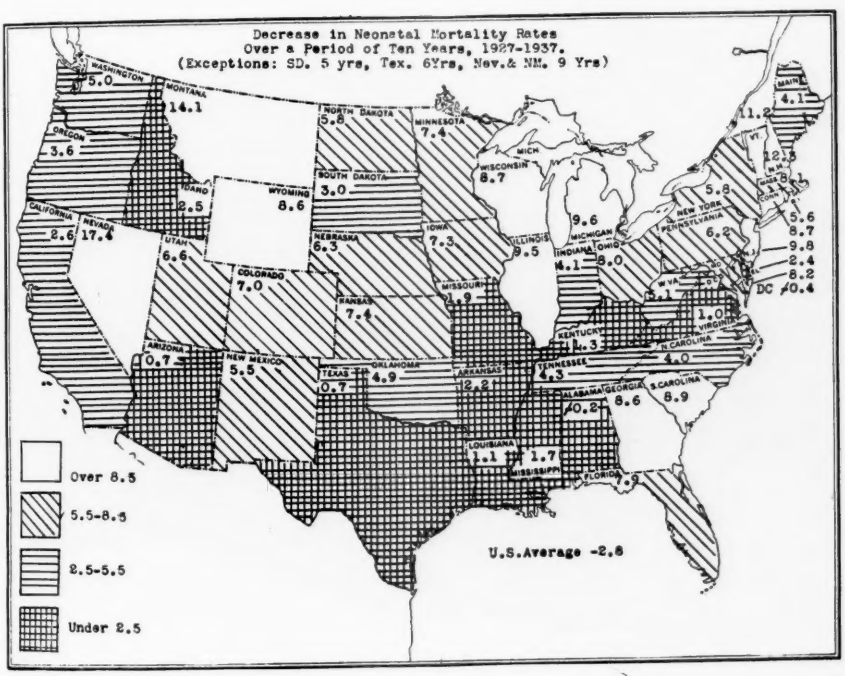


Chart 4.

In an effort to evaluate the various "probable causes of death" we proceed now with some further detailed data from the Ohio reports. It is fair to assume, considering the close correlation of Table II, that these figures are probably a fair sample of the entire United States. Total births in series were 39,821. In contrast to these figures which include only those infants whose deaths were due to prematurity, we have Table IV showing deaths from all causes arranged on the basis of fetal age. Not only is the mortality greater in earlier cases of prematurity but the ratio of stillbirths to neonatal deaths is higher.

It will be noted that in a considerable group of cases the method of delivery was not stated, hence the above percentages tend to be lower than the true figures. The interesting relationship between the deaths following spontaneous and forceps deliveries can of course be readily explained by the fact that practically all prema-

TABLE II

	CENSUS BUREAU			OHIO HOSPITALS	
Deaths due to dystocia		4,493	14.5%	127	11.9%
Breech presentation	764				
Other malposition	550				
Traumatism	632				
Deformed pelvis	359				
Other difficult labors	2,188				
Prolapse and compression of cord		3,343	10.8%	119	11.2%
Toxemia and albuminuria		2,260	7.3%	118	11.1%
Premature separation of placenta		2,207	7.1%	91	8.6%
Placenta previa		865	2.8%	30	2.8%
Death in utero (macerated 545)		1,807	5.8%	172	16.2%
Malformation		1935	6.3%	85	8.0%
Syphilis		666	2.2%	23	2.2%
Indefinite		4,393	14.2%	50	4.7%
Asphyxia, etc.	2,298				
Diseases of membranes	1,473				
Other specified cause	622				
Cause not specified	(6,662)	8,931	29.0%	249	23.3%
Abortion, etc.	2,269				
		30,900	100.0%	1,064	100.0%

TABLE III. PREMATURE BIRTH AS "THE PROBABLE CAUSE OF DEATH"

	NO. CASES	STILLBIRTHS	NEONATAL DEATHS	TOTAL DEATHS	MORTALITY
Prior to seventh month	319	87 (27.4%)	118 (37.0%)	205	64.4%
Seventh month	713	50 (7.0%)	171 (24.0%)	221	31.0%
Eighth month	696	8 (1.1%)	54 (7.8%)	62	8.9%
	1,728	145 (8.4%)	343 (19.9%)	488	28.3%
Incidence of prematurity 4.35 per cent					

TABLE IV. STILLBIRTHS AND NEONATAL DEATHS ACCORDING TO FETAL AGE

	NO. CASES	STILLBIRTHS	NEONATAL DEATHS	TOTAL DEATHS	MORTALITY
Prior to seventh month	319	185 (58.0%)	134 (42.0%)	319	100.0%
Seventh month	713	154 (21.6%)	232 (32.5%)	386	54.1%
Eighth month	696	117 (16.7%)	128 (18.4%)	245	35.1%
	1,728	456 (26.4%)	494 (28.6%)	950	55.0%
Term and not stated	38,093	608 (1.6%)	348 (0.9%)	956	2.5%
Total	39,821	1,064	842	1,906	

TABLE V. MATERNAL DISEASE IN RELATION TO DEATH OF CHILD

	NO. CASES	STILL-BIRTHS	NEONATAL DEATHS	TOTAL DEATHS	MORTALITY
Toxemia (Incidence 2.53%)	1,004	122	38	160	15.9%
Diabetes	23	4	6	10	43.5%
Syphilis	?	19	15	34	?

TABLE VI. FETAL DISEASE AS CAUSE OF DEATH

	NO. CASES	STILL-BIRTHS	NEONATAL DEATHS	TOTAL DEATHS	MORTALITY
Malformations (Incidence 1.35%)	535	85	113	198	37.1%
Erythroblastosis	25	3	9	12	48.0%
Enteritis	33	×	15	15	45.5%
Hemorrhagic disease of newborn	18	×	10	10	55.6%
Pneumonia	31	×	18	18	58.0%

TABLE VII. DISTRIBUTION OF INFANT DEATH BY METHOD OF DELIVERY

DELIVERY	NO. CASES	STILLBIRTHS		NEONATAL DEATHS		TOTAL DEATHS	MORTALITY
Forceps	18,070	174	(0.96%)	161	(0.89%)	335	1.85%
Spontaneous	18,482	404	(2.18%)	311	(1.67%)	715	3.85%
Cesarean section	947	48	(5.08%)	47	(4.95%)	95	10.03%
Pod. version	769	62	(8.09%)	35	(4.56%)	97	12.65%
Breech	1,456	111	(7.62%)	96	(6.59%)	207	14.21%
Craniotomy	19	19	(100%)			19	100.00%
Post mortem cesarean section and other operations	78	5		2		7	
Not stated		241		190		431	
Total	39,821	1,064	(2.69%)	842	(2.12%)	1,906	4.81%

tures, which contribute almost 58 per cent of the babies lost, are delivered spontaneously. On the other hand a great many forceps deliveries are purely elective and add no serious risk to the child.

In an effort to arrive at the relative incidence of fetal loss due to birth accidents in the various methods of delivery, an analysis of births at term where death was attributed to asphyxia, birth injury, or dystocia was made. This showed spontaneous delivery to have the lowest percentage incidence of fetal death (stillbirth and neonatal combined). Considering the incidence of death in spontaneous delivery as one, deaths following other delivery methods appeared in ratios as shown in Table VIII.

Returning to the Census Bureau reports we will consider the causes of infant deaths. Table IX lists all the deaths reported for the years 1936 and 1937, the latest at present available, compared with the deaths for the year 1930. Only

TABLE VIII. RATIO OF DEATH FROM INJURY BY METHOD OF DELIVERY

Spontaneous	1.0
Forceps	1.7
Cesarean section	6.6
Breech	8.3
Podalic version	16.8

the major causes are listed, the others being grouped under the heading "all other causes." However, no cause is excluded that had as many as 1,000 deaths in the first twelve months.

TABLE IX. MAJOR CAUSES OF INFANT DEATH. UNITED STATES, 1930, 1936, AND 1937

	IN FIRST MONTH			IN LAST ELEVEN MONTHS		
	1930	1936	1937	1930	1936	1937
Prematurity	35,290	32,452	32,524	1,466	1,191	1,133
Birth injury	10,475	9,502	9,496	151	148	102
Malformation	8,551	7,296	7,138	3,196	3,124	3,031
Debility	3,301	2,748	1,919	2,283	1,759	1,561
Pneumonia	3,440	2,972	2,990	12,749	14,775	13,577
Diarrhea	1,849	1,556	1,443	15,443	11,794	11,203
Influenza	366	419	493	2,459	3,082	3,226
Whooping cough	187	91	155	3,191	1,627	3,016
Syphilis	775	688	698	1,035	886	824
External cause	639	662	543	1,704	1,943	1,838
Unknown	5,222	4,269	3,990	3,582	2,704	2,667
All other causes	8,562	7,214	7,498	16,497	9,443	8,866
Total	78,657	69,869	68,887	63,756	52,476	51,044
Total births	2,233,958	2,144,798	2,203,337			
Rate per 1000	3.56	3.25	3.12	2.89	2.44	2.31

Several points are apparent. First, the figures on neonatal deaths have not made as marked an improvement as have the deaths in the later months. Second, the chief reasons for neonatal deaths are prematurity, birth injury, and malformation, in all of which the improvement has not been marked, and in which it cannot be expected that great savings could be made. Third, the great improvement in the deaths of later months has been in the infectious diseases, but even here those diseases that come in epidemics, pneumonia, influenza, and whooping cough, do not show constant decrease. While there should be continued improvement in the number of neonatal deaths, it cannot be expected to be as great as the improvement in the later months.

There are two factors, sex and race, that have a distinct bearing on infant deaths. Male babies die more frequently than female; this is true before as well as after birth.

TABLE X. EXCESS OF BIRTHS AND DEATHS OF MALE INFANTS. FIGURES TAKEN FROM THE CENSUS BUREAU STATISTICS FOR THE YEARS 1935, 1936, AND 1937. THE TOTAL BEING DIVIDED BY 3 TO PRODUCE THE ANNUAL AVERAGE

	LIVE BIRTHS	STILLBIRTHS (WHEN SEX REPORTED)	DEATHS DURING FIRST YEAR
Male	1,109,857	41,724	68,909
Female	1,054,449	32,559	51,959
Excess of males	55,408	9,165	16,950

Ratio of deaths by end of first year: male 3.97; female 3.00.

Of total pregnancies approaching term (sum of live and stillbirths) the death rate by end of first year is: male 95.5 per 1000; female 77.5.

Of total pregnancies approaching term male excess is	64,573	
By end of first year excess of male deaths is	26,115	40.4%
Excess of males at end of first year reduced to	38,458	

No explanation of these facts is presented, but the difference is very striking.

The factor of race is worthy of discussion. Both the stillbirth and the infant mortality rates are considerably increased because of the large number of infant

deaths occurring in the negro race. The stillbirth rate would be reduced from 33.3 to 29.2 if only the white stillbirths were taken into account. Considering negro births and stillbirths only, the rate is 63.2. Similarly the infant mortality rate is also affected. The 1938 rate for the United States is 51.0, the white rate being 46.0 and the negro rate 78.1. It is difficult to compare these rates state by state, because in many states there are few negro births, and where there are few births the rates lose in significance. However, of the states that have over 0.5 per cent of negro births a year, there are only four that have a negro infant mortality rate as low as the four states having the highest white rates. It is impossible to determine from these figures whether this poor record is inherent to the race, whether it is largely due to the type of care received by the negro, or whether it is due to the conditions under which he lives. There is much to argue against the first possibility in the fact that the white urban infant mortality in many of the southern states is very high. In fact in three of the states, the urban white infant mortality rate is worse than is the negro infant mortality for the same states (West Virginia, Alabama, and Mississippi). However, it is possible statistically to segregate the negro race and show that the large number of stillbirths and infant deaths which they contribute raise the average for the country considerably. It is more than possible that if certain other factors could be eliminated similar reductions could be expected.

SUMMARY

Attention is called to the marked discrepancies in the different states in the definition of the term "stillbirth," and a plea is made for conformity.

The definition of "neonatal death" is discussed. The number of stillbirths and neonatal deaths in the United States are analyzed with an attempt to fix the cause and age at occurrence.

The greater improvement in the later infant mortality over a period of years, as compared with the death rate of the newborn, is discussed.

The high incidence of death in negro babies is noted, and the higher mortality of male babies is demonstrated.

CONCLUSION

The considerable risk of deaths at the time of birth and shortly thereafter has been demonstrated. This risk is decreasing from year to year but not with great rapidity, because of the fact that some of the causes are not amenable to treatment. A better understanding of the factors involved may help to save many lives.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF APRIL 19, 1940

The following papers were presented:

The Coincidence of Tuberculosis of the Endometrium With Tuberculosis of the Lung. Drs. Julius E. Lackner, Walter Schiller, and Alex. S. Tulsky (by invitation). (For original article, see page 429.)

Effect of Vitamin K Administered to Patients in Labor. Drs. J. E. Fitzgerald and Augusta Webster (by invitation). (For original article, see page 413.)

Retrodisplacement of Uterus in Relation to Pregnancy. Dr. Albert H. Aldridge (by invitation). (For original article, see page 361.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Gynecologic Operations

Chavannaz, J.: Reflections on Vaginal Hysterectomy, Rev. franç. de gynéc. et d'obst. 33: 877, 1938.

Today vaginal hysterectomy has almost fallen into oblivion. In fact there are well-known surgeons who have not performed a single one of these operations and many surgeons have not even seen one done. Chavannaz discusses vaginal operations from his experience of twenty years.

There is no doubt that a vaginal hysterectomy can be performed much more rapidly than an abdominal hysterectomy. It can be done in eight to ten minutes and even less time. The risk of infection during the operation is certainly less than in cases of abdominal hysterectomy. If an infection does take place, drainage readily occurs and there is very little danger of general peritonitis. There is no postoperative scar and this is advantageous from an esthetic point of view.

The author favors the use of clamps and not ligatures. The clamps are left in place for forty-eight hours. His indications for the operation are as follows: prolapse of the uterus, small fibroid uteri and cases of metritis where radiotherapy is not advisable and certain cases of uterine and uteroadnexal infection. If a plastic operation is necessary, it is performed about three months after the vaginal hysterectomy.

The author maintains that with proper indications and technique the postoperative convalescence is comparable to that following a curettement. He believes that about 5 per cent of all hysterectomies should be performed by the vaginal route.

J. P. GREENHILL.

Faure, J. L.: Vaginal Hysterectomy, Bull. Soc. d'obst. et de gynéc. 27: 45, 1938.

During the past twenty-five years Faure has attempted to teach the technique of vaginal hysterectomy to his students. In spite of this, fewer of these operations are being performed. The author's chief indication for vaginal hysterectomy is infection of the uterus, because the vaginal route offers an excellent route for drainage. He has for many years advocated this operation for cases of puerperal infection in spite of the opposition of all obstetricians and many surgeons. The operation is also indicated in women who are exhausted, sometimes nearly dying, and in obese women. The operation is very well tolerated by all patients even when it takes a long time to complete. Where there are no complications, the operation requires only a few minutes. However, this is no reason to extend the indications to many other conditions such as extensive prolapse of the uterus except where there are serious pathologic changes in the uterus.

Faure believes that the simplest, cleanest, and most rapid technique of vaginal hysterectomy is Doyen's method of anterior hemisection. The only drawback of this operation is that it can be done only in cases where the uterus can readily be brought down. The operation can be done in five minutes.

J. P. GREENHILL.

Radford, Aubrey: Total Hysterectomy, South African M. J. 11: 232, 1937.

The view is presented that owing to the ease and safety of subtotal hysterectomy this procedure has been adopted too frequently and unjustifiably. The author pleads for a more widespread use of total hysterectomy via the vaginal route.

Plastic operations may be performed at the same time. The remaining cervix, in the subtotal hysterectomy, is a constant menace as an infective focus and often becomes the seat of carcinoma.

The author finds lumbar anesthesia ideal for vaginal hysterectomy.

F. L. ADAIR AND S. A. PEARL.

Haultain: The Treatment of Pyosalpinx, J. Obst. & Gynaec. Brit. Emp. **46**: 503, 1939.

This is a review of 84 cases of definite pyosalpinx, 54 cases being acute and 30 chronic; 22 were instances of tuberculous pyosalpinx. Of the 54 acute cases, 34 patients received conservative treatment; this, however, failed in 10 cases and an operation had to be undertaken.

Clinical cure occurred in 20 cases following conservative treatment alone, while two patients died, both being tuberculous.

Operation is advised in all cases in which conservative treatment fails or the patient has continued ill-health, is constantly miserable with pain or/and menorrhagia, is unable to work, to look after her household or even enjoy life on account of her pelvic condition; the operation generally indicated is hysterectomy with removal of both appendages.

Four cases of rupture or leak of a pyosalpinx were encountered, and there were 2 other cases in which at the operation the Fallopian tubes were found to be on the point of rupture: 3 of these patients died, and all would probably have been lost had not immediate operation been possible. Five deaths are recorded among the 30 patients operated upon, three from rupture or necrosis of the tubal wall, the other two being cases for which conservative treatment had been carried out too long before operation was done.

Results are given of 30 operations for chronic pyosalpinx, one death being recorded from embolism on the twenty-third day of an otherwise excellent convalescence. Details of the 22 tuberculous cases, including the late results, are given, 8 being acute and 14 chronic. Twenty patients were operated upon and the radical operation was performed in 13. Only one death is recorded in the operated cases, and this occurred in a patient who had mixed infection of gonococci and tubercle bacilli. There was no mortality in the cases which were purely tuberculous. The late results, up to seven years later, were found to be uniformly excellent in those treated radically, there being no apparent spread or exacerbation of tuberculosis elsewhere; whereas when some form of conservative operation was done, the health of 3 out of the 7 so treated was found to be adversely affected at a later date.

J. P. GREENHILL.

Schultz, W.: Pelvic Puncture, Zentralbl. f. Gynäk. **63**: 213, 1939.

Schultz first describes the technique of this operation; then discusses the indications. The chief use for this diagnostic procedure is to diagnose a tubal pregnancy. From 1919 to 1938 pelvic puncture was used to verify the diagnosis in 345 cases of ectopic pregnancy in the Hamburg Woman's Clinic. In 287 additional cases, an operation for tubal pregnancy was performed without a preliminary pelvic puncture, and in 14 cases, the puncture failed to give the desired information.

With the exception of blood in the peritoneal cavity due to endometriosis or rupture of an ovarian cyst, the aspiration of blood at the time of a pelvic puncture is definite proof of an ectopic pregnancy. If the tubal pregnancy is unruptured, no blood will be obtained.

Another indication for a pelvic puncture is the presence of an undefinable tumor in the pelvis. In 54 such cases the puncture resulted in a correct diagnosis 45 times. The material obtained by aspiration was fixed in alcohol and sectioned.

In the presence of gynecologic peritonitis, pelvic puncture has both diagnostic and therapeutic value. When inflammatory adnexa are present, pelvic puncture is

important for a correct diagnosis. However, pelvic puncture should not be used in acute cases, it should be reserved for subacute and chronic inflammatory tumors. Therapeutically the aspiration of the contents of inflammatory masses brings about a cure even if the entire contents of a cystic mass are not removed. For some reason, puncture of an inflammatory mass hastens absorption.

The author followed up a series of 301 women who had undergone a pelvic puncture for inflammatory masses at least five years previously. In 47 of these cases (15 per cent), pregnancy followed pelvic puncture and 31 of the women went to term. In 218 cases, complete cure resulted only in 36 cases, and in the others a second course of conservative therapy had to be instituted. Only 47 women had to be operated upon. These statistics support the author's contention of the great therapeutic value of pelvic puncture in cases where inflammatory masses are present.

In cases of pelvic abscess, the author advocates immediate incision and drainage of the cul-de-sac.

There are few dangers connected with pelvic puncture. In the series of more than 2,000 pelvic punctures performed in the author's clinic, the bowel was penetrated only between 20 and 30 times. This accident is entirely harmless. A more serious complication is bleeding, but this occurs almost exclusively if the puncture is made to one side instead of in the midline. However, nearly always the bleeding is external and can be controlled by packing the vagina or occasionally by using a suture. Intra-abdominal hemorrhage was never encountered. Another danger is rupture of a thin-walled abscess. This occurred once in this series. The author never saw an infection follow a pelvic puncture. Nevertheless he warns that this procedure should never be carried out in the office, but only in a place where a laparotomy may be performed if it should become necessary.

J. P. GREENHILL.

von Mihalkovics, E.: Simple Puncture as Palliative Therapeutic Treatment in Purulent Accumulations in the Female Pelvis, Monatschr. f. Geburtsh. u. Gynäk. **109:** 257, 1939.

In the opinion of the author, colpotomy should not be used when dealing with accumulations of pus in the adnexa because of the danger of subsequent fistula. This procedure is permissible only where death seems imminent. In cases of recent purulent inflammation the best treatment is aspiration of the pus by means of a syringe through the cul-de-sac. This simple procedure will bring about rapid improvement in three-fourths of all cases. It may also be carried out in cases of parametric abscesses and in infected hematoceles.

When there is an abscess in the cul-de-sac following salpingitis, a colpotomy should be performed because there is no danger of fistula formation. However, an incision is not necessary in these cases because aspiration gives just as good results.

J. P. GREENHILL.

Rubin, I. C.: Renal Tumor and Ectopic Kidney Associating or Simulating Uterine and Adnexal Tumor, Urol. & Cutan. Rev. **43:** 626, 1939.

Six cases of renal tumor and 3 cases of ectopic kidney were encountered by Rubin on the Gynecological Service at Mt. Sinai Hospital in the past eleven years in a series of 2,065 laparotomies. In 6 of the 9 cases the renal pathology was associated with genital pathology. In 3 the tumors simulated but were not confused with genital tumors. There were 3 renal cysts and 3 Grawitz tumors, one of which involved the ovary of the same side. There were 3 cases of sacral kidney, all 3 being found on the left side of the pelvis.

The rather uncommon occurrence of renal tumors in combination with genital tumors makes the diagnosis of the former a matter for special investigation. The renal tumor or anomaly was not primarily suspected in 5 of the 9 cases. Only

by x-ray study aided by intravenous injection of a radiopaque solution or by retrograde pyelography or by both procedures was the renal origin of the tumor determined.

The tumors encountered were of unusually large size reaching down into the pelvis where they were confused with tumors of the uterus or the adnexa. The routine use of x-rays in conjunction with pyelography, a practice which the author has adopted for some years in all large abdominal tumor cases, has led to correct preoperative diagnosis in 5 of the 6 renal tumor cases. The method of removal in 4 was by the transperitoneal route.

The diagnosis of sacral kidney is clinically only conjectural, the guess as a rule proving wrong. It is established by laparotomy or by x-ray study. In this connection a flat plate is not always reliable. Retrograde pyelography, ureteral catheterization, and intravenous urography yield pathognomonic evidence.

J. P. GREENHILL.

Lapeyre, N. D., Estor, H., and Gros, C.: Mikulicz Drainage in the Treatment of Tuberculous Salpingitis, Bull. Soc. d'obst. et de gynéc. **27:** 94, 1938.

In the service of the authors 22 patients with tuberculous salpingitis were operated upon. In the patients in whom they used a Mikulicz drain there was not a single case of persistant parietal fistula or a fecal fistula. In the literature the authors found reports of 98 patients treated by Mikulicz drainage alone. Among these patients there were 10 deaths, 9 uncomplicated cures, 8 temporary parietal suppurations, and 10 purulent fistulas which were spontaneously cured. These figures according to the authors do not indicate that Mikulicz drainage yields bad results but that tuberculous salpingitis is a grave disease. They strongly advocate the use of this type of drainage.

J. P. GREENHILL.

Barros, P.: The Baldy-Webster Operation by the Vaginal Route, Rev. de gynec. e d'obst. **1:** 261, 1939.

The author in general recommends the vaginal route for gynecologic operations. He describes the operation of round ligament shortening according to the technique of Professor Werner of Vienna. The description is made clear by the use of both black and white and colored drawings. In the article the author illustrates a special forceps designed by himself to facilitate grasping of the round ligaments.

MARIO A. CASTALLO.

Thalheimer and Contiades: Rupture of the Vaginal Scar after Hysterectomy, Gynéc. et obst. **35:** 299, 1937.

The patient, 50 years old, was brought to the hospital with severe vaginal bleeding which had come on suddenly while she was at stool. A loop of small intestine was found prolapsed into the vagina. She had had a little bleeding a few days previously after coitus. Total hysterectomy had been performed twelve years previously. The rupture was repaired by the abdominal route with recovery. The authors discuss the literature of rupture of vaginal scars. Coitus appears to be the commonest cause.

J. P. GREENHILL.

Beasley, B. T.: Altered Mechanics of the Female Pelvic Structures, South. M. J. **31:** 976, 1938.

The anatomic principles underlying the normal support of the female pelvic structures, and the mechanism whereby derangements occur, is briefly and concisely described.

Approximately 20 per cent of retroversions are congenital and occur in patients in whom the plane of the pelvic inlet lacks the normal incline. In such congenitally flat adult pelves, retroversion is normal and may be considered compensatory for the existing deviation from the more common and normal orthopedic condition. The function of the pelvic planes is supportive since the pelvic organs are held in place by the ligaments, and defensive in that they serve to deflect intra-abdominal pressure. Either one or both of these functions may be deranged by: (1) trauma (most common), (2) developmental errors, and (3) disease.

Simple, uncomplicated retroversions are symptomless. When symptoms are present, they are caused by complicating conditions. The complaints in congenital retroversion are due to attitudinal strain in the sacroiliac joints and erector spinae and psoas muscles. Uterine retroversion is followed by uterine prolapse of varying degrees, and this in turn is followed by descent of the bladder, vaginal vault, and cystocele formation. Upon the basis of incomplete evacuation of bladder contents cystitis develops.

The author urges that the fundamental principles of pelvic mechanics underly any corrective procedure indicated regardless of the specific operative technique employed. He offers three guiding principles: (1) An uncomplicated retroverted uterus does not need to be operated upon. (2) A congenital retroversion is not a gynecologic but an orthopedic problem. (3) No pelvic operation for the restoration of an organ is complete unless all defective supports are restored to their original equilibrium.

ARNOLD GOLDBERGER.

Malfanti, Juan: A New Technic of Hysteropexy, Bol. Soc. chilena de obst. y ginec. **4**: 275, 1939.

The essential features of the author's operation for the correction of retroversion and retrodisplacement involve a dissection into the broad ligament along a line just beneath the round ligament. The round ligament is divided midway between its uterine attachment and the internal inguinal ring. The free ends are overlapped sufficiently to bring the uterus into the desired degree of anteversion, and then sewed to each other. Complete peritonization is secured by enclosing the shortened round ligament within the dissected folds in the broad ligament.

In the discussion of the paper the chief objection made to the procedure was the likelihood of interference with the blood supply and consequent atrophy of the round ligaments with reccurrence of the retrodisplacement. Malfanti's statistics appear favorable. The article is illustrated.

R. J. WEISSMAN.

Ward, Grant E.: Ox Fascia Lata for Reconstruction of Round Ligaments in Correcting Prolapse of the Vagina, Arch. Surg. **36**: 163, 1938.

To Koontz (Ann. Surg. **83**: 525, 1936) belongs credit for devising a practical method of preserving fascia lata of the ox, so that it can be kept in the operating room for immediate use as any other suture material.

Ward describes in detail how in 1933 he made use of such prepared ox fascia in forming duplicate round ligaments for lifting up the short vagina which had prolapsed subsequent to a total hysterectomy for early adenocarcinoma. The operation took almost two hours. Patient made a smooth recovery and in 1937 still is well and free of any pelvic or bladder symptoms. The writer suggests that possibly in the same manner, preserved fascia lata could be used for correction of retroversion of a heavy uterus or in building up a weak pelvic floor.

HUGO EHRENFEST.

Decoulx, P. and Patoir, G.: Results of Conservative Surgery for Sclerocystic Oophoritis, Bull. Soc. d'obst. et de gynéc. **26:** 82, 1937.

The authors review a series of 200 cases of sclerocystic oophoritis. In 165 cases the treatment consisted of total or partial resection of the ovaries and in 35 cases also a hysterectomy was performed. There were two deaths following operation, one from embolism and the other from postoperative hemorrhage. There were bad results in 53 per cent of the cases. These consisted of persistent pain, irregular and painful menstruation, and impossibility of leading a normal existence. Furthermore 25 per cent of these women had to have a second operation. Good results were obtained in 47 per cent of the cases and 10 per cent of these had one or more babies following their operation.

J. P. Greenhill.

Hamant, A., Girard, G. and Soubiran: Two Cases of Residual Cysts After Hysterectomy, Compt. rend. Soc. franç. de gynéc. **8:** 223, 1938.

The authors report two cases where ovarian cysts appeared after hysterectomy. They believe the predisposing cause of these cysts lies in the local conditions such as previous inflammation, hence these cysts are frequently found in women who have had drainage after operation. In both of the authors' cases, drainage had been used.

The patients return after hysterectomy because of pain or because they have observed abdominal swelling. In some women, the cyst is discovered accidentally.

Unusually these cysts appear within one or two years after hysterectomy but in the authors' second case it appeared nineteen years later.

These cysts cannot be prevented because even if both ovaries are removed there may be a supernumerary ovary left behind. Moreover a simple hematoma may become a cyst or an infection may lead to cyst formation.

If a cyst is found in a woman who is near the menopause, it may be advisable to wait for it to disappear spontaneously, or radiotherapy may be used. The treatment of choice, however, is laparotomy.

J. P. Greenhill.

Knaus, Herman: A New Phenomenon Which Is an Accurate Indication for Surgical Interference in Peritonitis of Pelvic Origin, Klin. Wchnschr. **16:** 963, 1937.

Knaus has observed, for the last five years, a new phenomenon which occurs exactly at the time when the infection reaches the general peritoneal cavity. It consists in the complete absence of all respiratory movements of the abdominal wall between the umbilicus and the symphysis. Such respiratory movements stop long before the general signs of abdominal peritonitis set in. When observed, therefore, this phenomenon is a definite indication for immediate drainage of the abdominal cavity. Such early drainage has enabled the author to save many lives which would have been lost, if operation had been delayed until the standard signs of generalized peritonitis had set in.

Ralph A. Reis.

Schmid, H. H.: Prevention of Postoperative Thrombosis and Embolism, Zentralbl. f. Gynäk. **61:** 307, 1937.

At the meeting of the German Gynecological Society in 1935, it was reported that thrombosis and embolism could be prevented by the simple procedure of elevating the foot end of the bed after all extensive gynecologic operations. Now Schmid reports a series of 500 serious gynecologic operations in which this pro-

cedure was employed and in which there was not seen a single instance of thrombosis of legs or pelvic veins and not a single fatal case of pulmonary embolism. In contrast to this there is a series of 2,463 gynecologic operations performed before elevation of the foot of the bed was practiced. In this group there were 81 cases of thrombosis and 22 deaths from pulmonary embolism. No other explanation for the improved results could be found by the author, because no other changes have been made in the hospital routine. Even the type of anesthesia had remained the same, namely, preliminary use of pernocton followed by ether inhalation. In the 500 cases, the foot of the bed was elevated immediately after operation and this position maintained for four days. Elevation of the legs assists in the return flow of blood to the heart.

J. P. GREENHILL.

Charbonnier, A.: The Method of Getting Patients Out of Bed Early After Gynecologic Abdominal Surgery, Compt. rend. Soc. Franç de gynéc. 8: 314, 1938.

The author is in favor of getting patients out of bed early following abdominal operations for gynecologic disorders. However, exceptions to this practice are women in shock and those with drainage, hemorrhage, hypertension, and tachycardia. Likewise women with cardiac abnormalities, cachexia, severe infection and bedridden patients should be kept in bed a sufficiently long time after operation.

Women who are to get out of bed early are first made to exercise in bed even before operation in order to activate the circulation. These exercises include deep respiration and movements of the arms and legs. They are carried out daily from the day of operation until the patient leaves the hospital. On the third day after operation the patient is assisted to sit on the edge of the bed for five to fifteen minutes. On the fourth day she is helped to a chair where she remains for fifteen to sixty minutes. On the fifth day she takes a few steps in the room and stays up for one to two hours. On the sixth day she remains up for two to four hours. On the following days the patient may walk around in the halls and may walk up and down stairs.

Among 285 women who underwent this routine, there was not a single accident and only one case of phlebitis.

J. P. GREENHILL.

Correspondence

To the Editor:

In reading obstetric literature, I am struck with the diversity of meanings attached to the words "parous, primipara," etc. The word "parous" is used by some to designate "one who *has borne* a child," by others to mean "one who is *now pregnant*," and by still others "one who has been delivered of a *living* child." Thus a nullipara may be a woman who has never been pregnant, or one who is in her first pregnancy but not yet delivered, or one who has had any number of miscarriages. A primipara may be a woman who is in her first pregnancy, or one who has completed her first pregnancy, or one who has had one completed pregnancy with a living or dead fetus, according to the use of the word parous, and is now in her second pregnancy, or one who has had any number of miscarriages plus one living infant and is now in another pregnancy, or one who has had any number of miscarriages and is now in another pregnancy. The number of combinations is practically unlimited, and all may be found in obstetric literature. One woman referred to by an author as "para iii" was in reality in her *ninth* pregnancy. She had previously had three living children and five miscarriages.

With such a wealth of confusion in terminology, it becomes apparent that in order to have one's meaning unmistakable, one must further define just how many

pregnancies the woman has had if she is described as "para ii" for example. If such elaboration is necessary to make the use of the word "para" clear, would it not be preferable to leave out the "para ii" and let the explanation suffice? Thus a woman would not be "para i, para iii, or para ix," but she would be in her first, third, or ninth pregnancy, with so many miscarriages and so many living infants. Some writers will object that "para" is sanctioned by tradition, and should not be abandoned. It would appear impossible, however, to settle upon a meaning which would be adhered to by all writers. And is it worth while to continue the use of terms which are so obscure that at least two and perhaps a dozen meanings may be read into them? The purpose of scientific literature is to set forth a meaning that cannot be misunderstood, and of which there can be only one interpretation. No matter how hallowed the tradition, if it is obscure, it should be abandoned. It would be well if all obstetric texts and journals were to adopt a simple terminology, and if all medical students were to follow it, whereby a woman is described as "being in her first, or third, or ninth pregnancy," with all reference to "para" omitted. If this policy were adopted, the reader who is interested in the number of pregnancies which a mother has undergone who herself shows some condition attributable to childbearing, or who produces some malformation in her offspring thought to be dependent upon the number of times the mother has been pregnant, such a reader would have definite data for his study. At present, confusion in the mind of the reader, on such a simple matter as the number of pregnancies a patient of a colleague has undergone, is unavoidable.

MADGE THURLOW MACKLIN, A.B., M.D., LL.D.

University of Western Ontario Medical School, London, Canada.
August 10, 1940.

Items

Obstetrics and Gynecology in the Graduate Training Program of the American College of Surgeons

Of the 179 hospitals on the list approved for graduate training in general surgery and the surgical specialties by the American College of Surgeons, 73 have a program of training in either obstetrics or gynecology, or both, or the combined specialties. Those offering acceptable training in obstetrics number 12, in gynecology 8, and in obstetrics and gynecology 53. In training under approved programs are approximately 53 men in obstetrics, 19 in gynecology, and 234 in obstetrics and gynecology. Annually, 16 obstetricians complete two years, 3 complete three years, and 1 completes four or more years of training; 5 gynecologists complete two years, 2 complete three years, and 1 completes four or more years of training. For the combined specialties, 91 men are turned out each year, 84 of whom have had three years' training and 7 have had four or more years.

Affiliations with medical schools exists in the cases of 8 hospitals offering graduate training in obstetrics, 6 offering graduate training in gynecology, and 48 offering training in obstetrics and gynecology.

The graduate training committee of the College has felt it necessary to limit the approved list to hospitals where graduate training plans of three years for obstetrics and gynecology already existed or where immediate extension to three years was contemplated. When the training has been of particular excellence, a few exceptions to this rule have been made. However, when the training is for obstetrics or gynecology alone as separate specialties, it seems to be indicated that two years is considered acceptable.

The figures for approved training programs indicate the definite trend in recent years to combine these specialties, both from the educational standpoint and for the development of combined services in many medical schools and hospitals.

The leadership of medical schools in developing and guiding graduate training programs in these specialties is evidenced by the fact that all but 12 of the approved programs are in hospitals which have an affiliation with a medical school for graduate training purposes.

In only three instances is training in general surgery required in qualifying for appointment for graduate training in obstetrics and gynecology. It has also been unusual to find any exchange of residents between the departments of general surgery and obstetrics and gynecology in the hospitals that have been surveyed by the College. As the programs are at present formulated, in many hospitals little opportunity is provided for the future obstetrician and gynecologist to gain broad knowledge of some of the general surgical problems of the lower abdomen, or for the general surgeon in training to gain experience in gynecologic problems.

Three major types of basic science activity in graduate training programs in hospitals are recognized by the College; first, the practical study of surgical pathology; second, basic course—a more or less formal academic type of instruction; third, research. In 49 of the programs of training in obstetrics, gynecology, and the combined specialties, provision is made for practical study of surgical pathology; in 19 provision is made for a basic course, mostly on a part-time service arrangement; in 6, provision is made solely for research.

In obstetrics and gynecology, as in general surgery and the other surgical specialties, the objective of graduate training is the development of a surgeon having a thorough background of knowledge fundamental to his specialty and possessing skill in the techniques of his profession. One of the most important requisites of an effective program is a well-organized staff of exclusive specialists in their respective fields, having high scholastic and professional standing, and possessing the attributes of the teacher. Personal supervision and direction of the work of the resident staff by assigned personnel should obtain at all times. An outpatient department with systematic follow-up clinics is essential to a well-organized program. The resident staff should attend medical staff, departmental and clinicopathologic conferences, observe and participate in autopsies on the service, be responsible for some teaching activities, be directed in the study of the basic sciences and of scientific literature, and obtain sufficient operative experience under supervision to provide a reasonable degree of technical efficiency.

As a preliminary to a resident staff appointment, a candidate must be a graduate of an approved medical school and have had at least one year of interneship in a hospital providing acceptable interne training.

A list of the plans approved by the College for training in obstetrics and gynecology, and the separate specialties combined, follows:

Hospitals Approved for Graduate Training in Obstetrics and Gynecology By the American College of Surgeons

Los Angeles County Hospital
Los Angeles, Calif.
Stanford University Hospitals
San Francisco, Calif.
University of California Hospitals
San Francisco, Calif.
New Haven Hospital
New Haven, Conn.
Gallinger Municipal Hospital
Washington, D. C.
Grady Hospital (Emory University Service)
Atlanta, Ga.
University Hospital
Augusta, Ga.
Presbyterian Hospital
Chicago, Ill.
Research and Educational Hospitals of the University of Illinois
Chicago, Ill.
University of Chicago Clinics
Chicago, Ill.
University Hospitals
Iowa City, Iowa
University of Kansas Hospitals
Kansas City, Kan.
Louisville City Hospital
Louisville, Ky.
Charity Hospital of Louisiana
New Orleans, La.
Mercy Hospital
Baltimore, Md.
University Hospital
Ann Arbor, Mich.
Grace Hospital
Detroit, Mich.
Harper Hospital
Detroit, Mich.
Henry Ford Hospital
Detroit, Mich.

Receiving Hospital
Detroit, Mich.
Woman's Hospital
Detroit, Mich.
Minneapolis General Hospital
Minneapolis, Minn.
University of Minnesota Hospitals
Minneapolis, Minn.
Mayo Foundation for Medical Education and Research
Rochester, Minn.
Anker Hospital
St. Paul, Minn.
Firmin Desloge Hospital
St. Louis, Mo.
St. Louis City Hospital
St. Louis, Mo.
St. Louis Maternity Hospital
St. Louis, Mo.
Kings County Hospital (Kings County Division and Long Island College Division)
Brooklyn, N. Y.
Long Island College Hospital
Brooklyn, N. Y.
Edward J. Meyer Memorial Hospital
Buffalo, N. Y.
Bellevue Hospital (Third Surgical Division)
New York, N. Y.
Flower and Fifth Avenue Hospitals
New York, N. Y.
Lying-in Hospital
New York, N. Y.
Metropolitan Hospital
New York, N. Y.
Presbyterian Hospital
New York, N. Y.
Woman's Hospital
New York, N. Y.
Strong Memorial Hospital
Rochester, N. Y.
Duke Hospital
Durham, N. C.
City Hospital
Cleveland, Ohio
St. Luke's Hospital
Cleveland, Ohio.
University Hospitals of Cleveland
Cleveland, Ohio
University of Oklahoma, State University Hospital
Oklahoma City, Okla.
University of Oregon Medical School Hospitals and Clinics
Portland, Ore.
Hospital of the University of Pennsylvania
Philadelphia, Pa.
Jefferson Medical College Hospital
Philadelphia, Pa.
Kensington Hospital for Women
Philadelphia, Pa.
Elizabeth Steel Magee Hospital
Pittsburgh, Pa.
Vanderbilt University Hospital
Nashville, Tenn.
Baylor University Hospital
Dallas, Texas
State of Wisconsin General Hospital
Madison, Wis.
Toronto General Hospital
Toronto, Ont., Canada
Royal Victoria Hospital
Montreal, Que., Canada

Hospitals Approved for Graduate Training in Obstetrics

Touro Infirmary
New Orleans, La.
Baltimore City Hospitals
Baltimore, Md.
Johns Hopkins Hospital
Baltimore, Md.
Sinai Hospital
Baltimore, Md.
University Hospital
Baltimore, Md.
Boston Lying-In Hospital
Boston, Mass.
Massachusetts Memorial Hospitals
Boston, Mass.
Margaret Hague Maternity Hospital
Jersey City, N. J.
Cincinnati General Hospital
Cincinnati, Ohio
John Gaston Hospital
Memphis, Tenn.
Medical College of Virginia
Richmond, Va.
University of Virginia Hospital
University, Va.

Hospitals Approved for Graduate Training in Gynecology

Johns Hopkins Hospital
Baltimore, Md.
University Hospital
Baltimore, Md.
Free Hospital for Women
Brookline, Mass.
Albany Hospital
Albany, N. Y.
Buffalo General Hospital
Buffalo, N. Y.
Mount Sinai Hospital
New York, N. Y.
Graduate Hospital of the University of Pennsylvania
Philadelphia, Pa.
John Gaston Hospital
Memphis, Tenn.

American Board of Obstetrics and Gynecology

The annual written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 4, 1941, at 2:00 P.M. Candidates who successfully complete the Part I examinations proceed automatically to the Part II examinations held later in the year.

The following action regarding case records to be submitted by candidates taking the Group B, Part I, examination was passed by the Board at its annual meeting in Atlantic City, N. J., on June 6, 1940: "Case records submitted by candidates must be of patients treated within four years prior to the date of the candidate's application. The number of cases taken from one's residency service should not be more than half (25) of the total number of fifty (50) cases required."

Applications for admission to Group B, Part I, examinations must be on file in the Secretary's Office not later than October 5, 1940.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Cleveland, Ohio, immediately prior to the June, 1941, meeting of the American Medical Association.

After January 1, 1942, there will be only one classification of candidates, and all will be required to take the Part I and Part II examinations.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

Training Requirements

In response to numerous inquiries regarding special training requirements, the Board desires again to announce that there are three methods of meeting these requirements for admission to the Board examinations. First, by the residency system; second, by the partial residency and partial assistantship method; and third, entirely by the assistantship or "preceptorship method." Details of the residency requirements are given in the Board booklet. The Board will accept in lieu of the formal residency service the training acquired by a candidate serving on an assistant or dispensary staff of an obstetrical and gynecological division of a recognized Hospital, under the direction of a recognized obstetrician-gynecologist (preferably a Diplomate). The time required for this type of training must be longer than with the formal, more intensive residency type of training, and the allowance of time depends upon the duties and responsibility given the candidate. Applicants lacking all formal special training should have a minimum of five years of hospital clinic, or assistant staff appointments in the specialty, under approved direction. Teaching appointments without accompanying hospital staff or clinical appointments will not satisfy the Board requirements. A special form amplifying the original application must be filled out to cover the details of such assistantship, or preceptorship type, of training. The Board approves for special training, work done in institutions approved jointly by the Board and by the Council on Medical Education and Hospitals of the A. M. A.

PAUL TITUS, SECRETARY.

1015 Highland Bldg., Pittsburgh, Pa.

Central Association of Obstetricians and Gynecologists

The twelfth annual meeting will be held at the Hotel Lincoln, Indianapolis, Ind., on October 10, 11, and 12, 1940. The guest speaker will be Dr. Robert Meyer, now of Minneapolis. The meeting is open to all physicians, without any registration fee.

American Journal of Obstetrics and Gynecology

OFFICIAL ORGAN

THE AMERICAN GYNECOLOGICAL SOCIETY
THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS, AND ABDOMINAL SURGEONS
NEW YORK OBSTETRICAL SOCIETY; OBSTETRICAL SOCIETY OF PHILADELPHIA
BROOKLYN GYNECOLOGICAL SOCIETY; ST. LOUIS GYNECOLOGICAL SOCIETY
NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY
BALTIMORE OBSTETRICAL AND GYNECOLOGICAL SOCIETY
CHICAGO GYNECOLOGICAL SOCIETY; CINCINNATI OBSTETRIC SOCIETY
CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS
AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY
WASHINGTON GYNECOLOGICAL SOCIETY
PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY
OBSTETRICAL SOCIETY OF BOSTON
LOUISVILLE OBSTETRICAL AND GYNECOLOGICAL SOCIETY
SOUTH ATLANTIC ASSOCIATION OF OBSTETRICS AND GYNECOLOGY

AMERICAN JOURNAL of OBSTETRICS & GYNECOLOGY

This issue commemorates its twentieth anniversary

1920 1940

OCTOBER


BIRTH
PRELUDE